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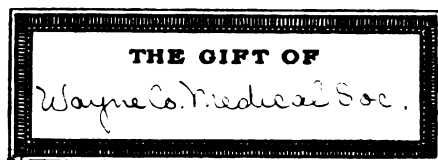
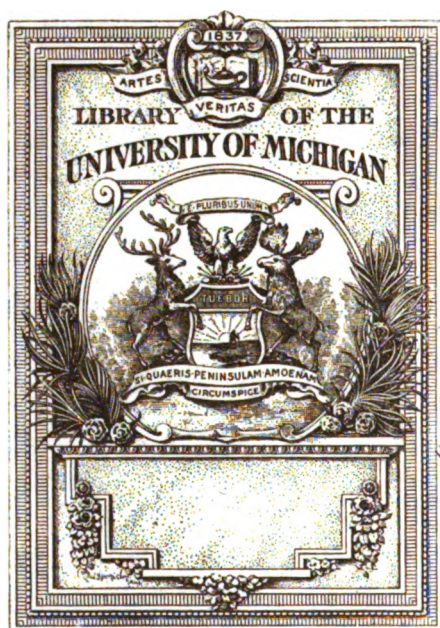
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FIG. 1

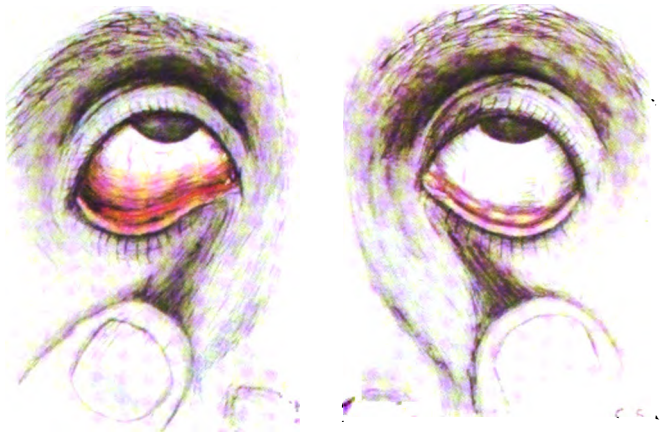


FIG. 2

FIG. 3

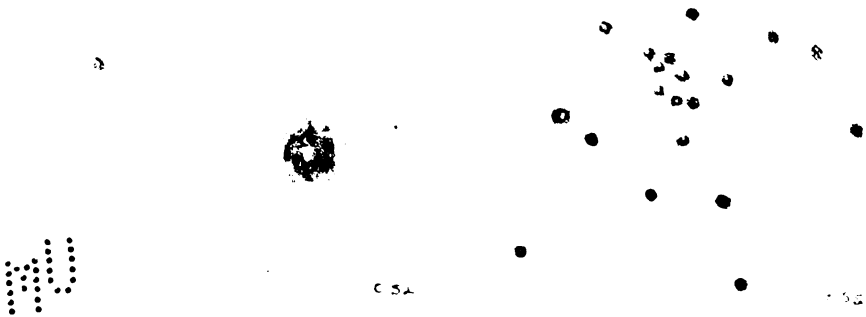


FIG. 1. Ocular tuberculin reaction

FIG. 2. Von Pirquet's cutaneous tuberculin test: control (negative) reaction, above and to the left; positive reaction, below and to the right

FIG. 3. Moro's cutaneous tuberculin reaction [*See points of contact*]

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
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ON

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PATHOLOGY, DERMATOLOGY, OPHTHALMOLOGY,
OTOLOGY, RHINOLOGY, LARYNGOLOGY,
HYGIENE, AND OTHER TOPICS OF INTEREST
TO STUDENTS AND PRACTITIONERS**

**BY LEADING MEMBERS OF THE MEDICAL PROFESSION
THROUGHOUT THE WORLD**

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CONTENTS OF VOLUME I

(TWENTIETH SERIES)

SPECIAL ARTICLES

	PAGE
THE SERUM DIAGNOSIS OF SYPHILIS. By HOMER F. SWIFT, M.D. . .	1
FURTHER STUDIES ON THE SERUM DIAGNOSIS OF SYPHILIS WITH ESPECIAL REFERENCE TO THE ANTIHUMAN HÆMO- LYTIC SYSTEM. By HIDEYO NOGUCHI, M.D.	22
THE NEWER DIAGNOSTIC METHODS OF SYPHILIS OF THE NER- VOUS SYSTEM. By B. SACHS, M.D.	32

DIAGNOSIS AND TREATMENT

SYMPTOMATOLOGY OF PELLAGRA. By J. J. WATSON, M.D.	42
THE TREATMENT OF PELLAGRA. By JAMES M. KING, M.D.	58
THE TUBERCULINS AND THEIR DIAGNOSTIC AND THERAPEUTIC USE. By JOHN BENJAMIN NICHOLS, M.D.	62

MEDICINE

SOME RECENT ADDITIONS TO OUR KNOWLEDGE OF PURIN ME- TABOLISM AND THEIR BEARING ON THE PROBLEMS OF GOUT. By H. GIDEON WELLS, PH.D., M.D.	76
CHRONIC MUCOUS COLITIS. By DUDLEY FULTON, M.D.	95

SURGERY

THE DIAGNOSTIC VALUE AND THERAPEUTIC EFFECTS OF THE BISMUTH PASTE IN CHRONIC SUPPURATION. By EMIL G. BECK, M.D.	102
TUBERCULOSIS OF THE THYROID GLAND, WITH REPORT OF A CASE. By A. E. HALSTEAD, M.D.	120

GYNÆCOLOGY

PROGRESS OF GYNÆCOLOGY AND ABDOMINAL SURGERY DURING THE LAST TWENTY YEARS. By A. LAPHORN SMITH, B.A., M.D., M.R.C.S., (Eng.)	126
THE HYGIENE OF MENSTRUATION. By ERNEST BOYEN YOUNG, M.D..	145

PÆDIATRICS

	PAGE
EYE-STRAIN AMONG SCHOOL CHILDREN. By AARON BRAY, M.D.	149

NEUROLOGY

TABES DORSALIS—ITS RATIONAL TREATMENT IN THE LIGHT OF ITS REAL PATHOGENESIS. By TOM A. WILLIAMS, M.D., C.M. (Edin.).	157
--	-----

ANATOMY

INVESTIGATION OF THE PORTIO VAGINALIS OF THE UTERUS IN RELATION TO CONCEPTION. By JUNE KICHI KIMURA, M.D. ..	171
--	-----

MISCELLANEOUS TOPICS

THE COURSE OF POSTGRADUATE STUDY OF THE AMERICAN MEDICAL ASSOCIATION. By JOHN H. BLACKBURN, M.D.	188
---	-----

PROGRESS OF MEDICINE DURING THE YEAR 1909

TREATMENT. By A. A. STEVENS, M.D.	193
MEDICINE. By JOHN H. MUSSEY, M.D. and LUCIUS TUTTLE, M.D.	228
SURGERY. By JOS. C. BLOODGOOD, M.D.	252

LIST OF ILLUSTRATIONS TO VOLUME I

(TWENTIETH SERIES)

COLORED PLATES

	PAGE
Ocular tuberculin reaction, Fig. 1; Von Pirquet's cutaneous tuberculin test, Fig. 2; Moro's cutaneous tuberculin reaction, Fig. 3..... <i>Frontispiece</i>	
Blood-collecting tubes (Fig. 1).— <i>a</i> , tube; <i>b</i> , same, ready for transportation; <i>c</i> , <i>d</i> , simple method of collecting blood.....	22
Blood-collecting tubes (Fig. 2).— <i>a</i> , <i>b</i> , with specimens of blood; <i>c</i> , <i>d</i> , taking out serum and placing in hæmolytic test-tube.....	22
Blood-collecting tubes (Fig. 3).— <i>a</i> , suspension of red corpuscles; <i>b</i> , hæmolysis of corpuscles; <i>a'</i> , corpuscles settled to bottom; <i>b'</i> , hæmoglobin shows no change.....	23
Appearance of all the blood-collecting tubes after the first incubation and just at the moment when the amboceptor slip is about to be added (Fig. 4)	23
Appearance of the tubes after completion of hæmolysis (Fig. 5).....	24
Appearance of the tubes shown in Fig. 5 after standing for several hours (Fig. 6)	24

PLATES

Lesions of pellagra on the face, arms, and hands (Fig. 6).....	54
Line of demarcation, "pellagra mark," on skin of neck (Fig. 7).....	54
Pellagra eruption, showing symmetrical arrangement (Fig. 8).....	54
Pellagra for five years—negro boy (Fig. 9).....	55
Pellagra—eruption most marked on lower part of legs (Fig. 1).....	60
Pellagra, showing dermatitis of areas not protected by clothing (Fig. 2)...	60
Pellagra of hands and arms in acute active stage (Fig. 3).....	60
Pellagra of hand, showing a larger degree of amplification than in Fig. 3 (Fig. 4)	60
Pellagra of feet (Fig. 5).....	61
Metal and glass syringes used for bismuth paste injection (Fig. 1).....	104
Stereoscopic prism glasses (Fig. 2)	104
Renal sinus disclosed by paste injection (Fig. 3).....	104
Liver abscess following appendicitis, paste showing communication (Fig. 4)	104
Double psoas abscess without destruction of vertebræ (Fig. 5).....	105
Rectal fistula originating in pelvis—closure by bismuth (Fig. 6)	105
Unsuspected origin of sinus opening at hip located by paste injection (Fig. 7)	106
Foreign body cause of failure of paste treatment (Fig. 8).....	110
Foreign body in humerus before injection of the paste (Fig. 9).....	110
Back of foreign body not reached by paste (Fig. 10).....	110
Stereoscopic empyema; Estlander operation two years ago; closure by paste treatment (Fig. 11).....	110
Bronchial tree of cat injected with bismuth paste (Fig. 12).....	110
Spondylitis, sinus sixteen years; closure after three injections of bismuth paste (Fig. 13).....	111
Prophylactic method of paste injection (Fig. 14).....	111
Sinuses of hip-joint filled with large quantities of paste causing bismuth poisoning (Fig. 15).....	116

	PAGE
Tuberculous knee-joint and eight sinuses; incurable with paste; amputation (Fig. 16)	116
Cut-sections showing condition in <i>tabes dorsalis</i> (Figs. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 19a, 20, 21, 22)	168
Section showing spherical form of cervix uteri (Fig. 1); conical form (Fig. 2); screw-head form (Fig. 3)	176
Iron bed in position on springs of ward bed (Fig. 1)	254
Wooden bed—ease with which heavy patient is kept sitting (Fig. 2)	254
Wroth's apparatus for proctolysis (Fig. 3)	255
X-ray of giant-cell sarcoma of lower end of radius (Fig. 4)	264
Recurrent epulis (Fig. 5)	266
Periosteal osteosarcoma of lower jaw (Fig. 6)	266
Alcohol specimen of carcinoma of gum of upper jaw (Fig. 7)	267
Patient from whom specimen shown in Fig. 7 was removed (Fig. 8)	267
Method of including inverted ends of descending colon and rectum in suture of parietal peritoneum of wound (Fig. 9)	270
Sketch of lateral anastomosis of smaller descending colon and larger rectum (Figs. 10 and 11)	270
Obstructive jaundice and gall-bladder tumor resembling clinically carcinoma of pancreas (Fig. 12)	286
First step of retrocolic cholecystenterostomy (Fig. 13)	286
Cholecystenterostomy—retrocolic cystenterostomy (Fig. 14)	286

FIGURES

Bacteriolytic system: bacterium, amboceptor, and complement (Fig. 1); these three united (Fig. 2)	2
Hæmolytic system: red blood-cell, hæmolysin, and complement (Fig. 3); these three united (Fig. 4)	2
Position of complement and antigen when no immune bodies are present (Fig. 5)	3
Complete syphilitic system (Fig. 6)	3
Temperature charts in pellagra (Figs. 1, 2, 3, and 4)	49
Clinical chart of a case of pellagra (Fig. 5)	53

Special Articles

THE SERUM DIAGNOSIS OF SYPHILIS

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THE subject of the serum diagnosis of syphilis falls naturally into two main divisions: (a) *Theoretical and Technical*; (b) *Practical Application of the Reaction*.

Under the first heading I shall discuss briefly: First, the principles upon which the method is based; second, the theories of the nature and mechanism of the reaction; third, its various modifications.

THEORETICAL AND TECHNICAL

The reaction is founded upon the Bordet-Gengou phenomenon, which demonstrates the presence of immune bodies by the fixation of complement. To understand this, it is necessary to review certain phases of immunity. An antigen is a substance which has the power of exciting the formation of antibodies when it is introduced in a suitable manner into a susceptible animal. If a horse, for example, be injected with increasing quantities of cholera vibrios (antigen), its serum develops the power of dissolving these organisms. This dissolving or lytic power is dependent upon two substances. One of these, the bacteriolysin or bacteriolytic amboceptor, is produced as a result of the immunizing process. It is called *amboceptor* because it has a double affinity. By its specific receptor it attaches itself to the antigen, and by the other to the second necessary substance, the complement. Complement is present in all normal sera. Its function is to complete the action of the amboceptor, and only when both amboceptor and complement are present does lysis of the cholera vibrios occur. These two bodies have

different physical properties; the amboceptor resists heating to 56°C . and hence is thermostabile, while the complement is destroyed by such heating, or by standing some days, and is therefore thermolabile. The heating to 56°C . is the process of inactivating, by means of which an immune serum can be obtained free from complement. Such a serum will not act alone, but if some fresh normal serum be added, the immune serum is reactivated. The three substances, bacterium, amboceptor, and complement, form the bacteriolytic system, and are represented in Fig. 1. When mixed in the proper proportions, and incubated at body temperature, they may be supposed to unite as shown in Fig. 2.

Hæmolysis may be explained in a similar manner. An animal (*A*), when injected with the red blood-cells from an animal of another species (*B*), develops in its serum the power of dissolving

FIG. 1.

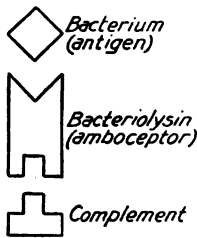


FIG. 3.

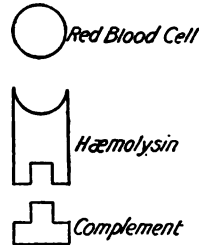


FIG. 2.



FIG. 4.



the red cells from animal *B*. Here, as in the case of bacteriolysis, the action is dependent upon, first, a specific amboceptor, the hæmolysin, which has the same physical properties as the bacteriolysin, and, second, the complement, which is identical with that which acted in the bacteriolytic system. The hæmolytic system is represented in Fig. 3.

When the members of this system are mixed and incubated, the cells become dissolved, which is shown by the clear red color of the solution in which they were mixed. Here the union would be pictured as in Fig. 4. Because many bacteria will not undergo lysis, Bordet and Gengou devised the following scheme to demonstrate the presence of immune bodies. The bacteria (antigen), the serum under examination (in which the complement had been destroyed by heating to 56°C .), and fresh complement were mixed and incubated. If the immune bodies were present a binding

occurred as shown in Fig. 2. If the immune bodies were not present to cause binding the complement and antigen would remain free in the solution as shown in Fig. 5.

To determine whether the complement was free or not they added red blood-cells and hæmolsin. If the complement had been bound to antigen by bacterial immune body, hæmolysis would not take place, and the red blood-cells would sink to the bottom of the test-tube. On the other hand, if no immune bodies were present the complement being free would unite with the other two members of the hæmolytic system, as pictured in Fig. 4, to produce hæmolysis, shown by the laked color of the fluid.

This method was devised to prove the unity of complement by showing that the complement would act in either lytic system, but it was soon demonstrated that immune bodies could be detected even when the micro-organisms were not dissolved by the immune serum.

FIG. 5.

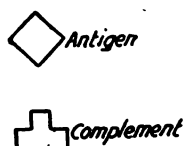


FIG. 6.



The diagnostic importance of such a reaction became evident. By means of it Bordet and Gengou demonstrated specific immune bodies in the serum of animals immunized to various bacteria, and in patients suffering from typhoid fever. These workers used whole bacteria in performing the reaction.

Gay noted that the period of fixation of complement was accompanied by a precipitate, and attributed the fixation of complement to the formation of this precipitate. To disprove this hypothesis, Wassermann and Bruck made watery extracts of bacteria for use as antigen, and with these extracts they proved the fixation of complement without the presence of a precipitate. With such a method for making a uniform extract the reaction assumed more diagnostic importance, and was used both to demonstrate the presence of immune bodies in specific infectious diseases, and to determine specific antigens by employing specific sera against doubtful antigens. They next made watery extracts of tuberculous organs,

which reacted in the fixation test, thus proving that organ extracts could be used in place of bacterial extracts. This was of importance because organ extracts could be used in the study of those diseases in which the etiological agent could not be artificially grown. It was but a step to the study of syphilis. By using watery extracts of livers from congenital syphilitics, Wassermann, Neisser and Bruck demonstrated complement-binding bodies in the blood of apes infected with syphilis. Because watery extracts from normal livers and sera from normal apes did not react, they concluded that the fixation was due to a specific immune body. Similar observations on the blood of syphilitics and the spinal-fluid of tabetics and patients with general paralysis confirmed this view.

The wide-spread interest in such an important reaction soon led to other discoveries. It was shown that watery extracts of malignant tumors and of normal organs reacted as antigens, though larger quantities of these substances were required. Next it was demonstrated that alcoholic extracts of both syphilitic and normal organs could be used as antigens. The substitution of various lipoid substances, such as lecithin, cholesterin, sodium glycocholate, sodium taurocholate, sodium oleate and oleic acid, in the pure state, all gave the reaction, though not as satisfactorily as total extracts.

This reaction between known pure, non-specific lipoids and some specific substance in syphilitic serum proved that the latter was different from the ordinary immune body. A number of theories have been advanced to explain the phenomenon.

Kraus and Volk determined that both the organ extract and syphilitic serum were *anticomplementary*, causing a non-specific destruction of complement, and attributed the reaction to a summation of anticomplementary action. Bauer holds similar views. The fact that at times one-fourth of the anticomplementary dose of each substance when mixed will bind complement destroys this view.

Wassermann advances the hypothesis that the antibody is a toxin which has marked affinity for lecithin and forms a toxolecithid, similar to the cobra-lecithin of Kyes and Sachs. Along similar lines Citron suggests that in the serum are two substances, first, a true antibody, the reagin; and, second, some soluble portion of the syphilitic virus. These two can unite only when there is a suitable lipoid to join them. This lipoid is obtained from the organ

extract, and when the three unite in the presence of complement they bind that complement. The complete syphilitic system is represented in Fig. 6.

Elias, Porges, Neubauer, and Salomon believe that the complement is bound by the precipitate which is formed by the union of lipoid with some substance in the syphilitic serum. The formation of this precipitate was demonstrated by Porges and Meier, and suggested as a diagnostic test, but as it is formed with sera from non-luetic patients it has little diagnostic value. Sachs shows that both the formation of a precipitate and the complement fixation occur best in unheated syphilitic serum; both are diminished or prevented by adding a weak alkali to the serum, and the addition of weak acid to such an alkaline serum favors the formation of a precipitate and causes a negative fixation test to become positive. The parallelism between the two phenomena is quite suggestive that the two reactions are closely allied. Liefmann lately advances the following argument in favor of the precipitation hypothesis: He says that if one accepts this view one must suppose a precipitable substance in the syphilitic serum and a precipitating substance in the organ extract. Substitutes for an organ extract must contain similar precipitating bodies. Sachs had previously shown that a precipitate is formed with the soaps as well as with lecithin and the bile salts. Both normal and syphilitic livers contain lecithin and bile salts, but Liefmann demonstrates that watery extracts of syphilitic livers contain three times as much soap as similar extracts from normal livers. To this fact he attributes the greater activity of the syphilitic watery extracts. They not only have a large soap content to form precipitates, but this soap makes an emulsion which brings the other lipoids into suspension in greater quantities than in extracts from normal organs. If the precipitation hypothesis is true, an acid medium is necessary for the reaction, and Liefmann found that the mixture of lues serum, organ extract and guinea-pig serum was equal to 0.3 c.c. $\frac{N}{10}$ HCl. The mixture never was alkaline. He further demonstrates that it is a precipitable portion of the complement which is specially affected in the fixation reaction. Ferratas had previously shown that complement is composed of two parts which can be separated when the salts are removed from the serum by dialysis. In such a dialysed

serum the globulin fraction is precipitated while the albumins and lipoids remain in solution. Neither the precipitate nor soluble portion can act alone as complement, but when they are mixed in a saline solution the mixture becomes slowly active. Liefmann precipitated the globulins in guinea-pig serum by means of carbonic acid and poured off the soluble portion. He then made the following mixtures:

- a. Lues serum + lues extract + globulin complement.
- b. Lues serum + lues extract + soluble complement.
- a'. Soluble complement + hæmolysin + sheep red blood-cells.
- b'. Globulin complement + hæmolysin + sheep red blood-cells.

The four mixtures were incubated one hour, after which *a* was added to *a'*, and *b* to *b'*, and again incubated. No hæmolysis occurred in *a a'*, and complete hæmolysis took place in *b b'*. Therefore the globulin must have been the portion bound.

To fully prove the precipitate binding theory, two facts must be established: First, that precipitation and fixation are parallel; second, that the different precipitating lipoids and normal extracts give as good fixation reactions as syphilitic extracts. The first point is definitely decided in the negative. Many sera, most often from tuberculous patients, do not give a fixation reaction with organ extracts, but give a precipitate with lipoids. If, as is claimed, this precipitate is due to an increase in the globulins, such an increase is frequently found in many other immunizing processes, and these non-syphilitic immune sera do not give a positive fixation with syphilitic extracts. A review of the work done as to the second point shows that the various lipoids which give a precipitate do not act as well as total extracts in the fixation test. For example, taurin acts well as a precipitant, but has practically no value as antigen in the Wassermann reaction. Whether alcoholic extracts of normal organs are as sensitive as those from syphilitic organs is still an open question. In my experience, the syphilitic extracts have been the best.

The following experiments of Bruck show that the "immune body" in syphilitic serum is not protective in nature.

1. An ape was treated with an extract of luetic organs, and a

fair antibody content determined with a Wassermann reaction. Inoculation with fresh syphilitic virus gave a typical chancre.

2. An animal was injected subcutaneously with 10 to 20 c.c. of positively-reacting serum, and at the same time inoculated on the eyebrow with syphilitic material. The inoculation was successful.

3. A similar result was obtained although the serum was injected under the site of inoculation.

4. Two cubic centimetres of strongly positive inactivated serum and 2 c.c. of fresh normal ape serum (complement) were placed in contact with the virus and incubated one hour. This virus when inoculated into a susceptible animal gave rise to a typical chancre.

The injections of apes with extracts of syphilitic livers never gave rise to as high an antibody content as the infection with fresh syphilitic virus. For this reason Bruck expresses the following opinion: "The antigen (exciter of complement binding antibody) does not originate directly from the causative agent of syphilis, but there is some unknown substance in the normal organs which undergoes an increase under the influence of the syphilitic virus, and then gives rise to the formation of antibodies."

This short résumé gives some idea of the divergence of opinion as to the nature of the reaction. Each hypothesis has its strong and weak points, and probably the true nature of the fixation will not be determined until the *Spirochæta pallida* can be grown in large quantities in pure cultures.

Let us now turn to the method itself with its various modifications. In Wassermann's original method, the following substances are required: (a) Patient's serum; (b) complement; (c) antigen; (d) hæmolysin; (e) red blood-cells from a sheep. These reagents are obtained and prepared for use as follows:

a. Patients' Serum.—From 2 to 5 c.c. of blood is collected in a sterile test-tube from the lobe of the ear, or by means of venous puncture. It is allowed to stand over night or until the serum separates from the coagulum. The serum is pipetted into a clean tube and inactivated by heating one-half hour in a water bath, at 56° C.

b. Complement.—A guinea-pig is anæsthetized and bled into a Petri dish by severing all the vessels of the neck. This blood is allowed to stand over night in the ice-chest, and in the morning the serum is poured off. It is best when slightly red, and more

uniform results are obtained if the serum from two or three pigs is massed. For use, one part of the serum is mixed with nine parts of normal salt solution, thus making a 10 per cent. mixture.

c. Antigen.—Wassermann's first method is to use a watery extract of syphilitic fetal liver. One Gm. of liver is finely ground and shaken for 24 hours with 5 c.c. of salt solution, to which 0.5 per cent. phenol has been added. It is then centrifuged to clearness and kept in the ice-chest. The proper amount of such an extract is one-half the "under inhibiting dose." For example, if it is found that 0.5 c.c. inhibits the action of the amount of complement used, while 0.4 c.c. does not, then 0.2 c.c. is the amount to use in the reaction. On account of the liability of this form of extract to change, this determination must be made each day before the regular reaction is tried. The alcoholic extracts are more stable, and just as reliable when properly standardized. The formula of Michaelis and Lesser is the most convenient. Syphilitic or normal liver or heart is finely ground and placed in ten volumes of absolute alcohol. The extraction is made by shaking for 24 hours at room temperature, or by allowing to stand at 37° C. for five to ten days, and shaking two or three times each day. It is then filtered and the alcoholic filtrate kept as a stock solution. For the test, an emulsion is prepared by adding one part of the alcoholic solution to four parts of salt solution and shaking. Before a new antigen is adopted, it should be standardized by comparing it with a known standard antigen. If the new extract is too strong it can be diluted; if it is too weak some of the alcohol can be evaporated until a proper strength is obtained. The alcoholic extracts are not subjected to the same rule for dosage as the watery antigens, because double the optimum dose of certain extracts alone are hæmolytic. Double the amount of alcohol alone will have an inhibiting effect unless the amount of salt solution in which the dilutions are made is also increased. In using alcoholic extracts the total amount of dilution should be more than ten times the amount of alcohol in the extract. If one doubles the alcoholic extract without taking cognizance of this fact, he will find complete inhibition, while if he doubles the diluting fluid at the same time there will be no anticomplementary effect from the extract.

d. Hæmolysin.—A rabbit is injected intraperitoneally, at inter-

vals of four days, with increasing quantities of sheep red blood-cells which have been washed three times. One usually begins with 4 c.c. of the washed cells and increases the quantity up to 20 c.c. Four injections usually produce a serum of high titre. Eight days after the last injection the rabbit is bled and the serum separated from the coagulum, after which it is inactivated and the unit determined. Diminishing amounts of the hæmolytic serum are put in several tubes, to each tube is added one unit of complement and one unit of cells and the total volume of all the tubes made the same. The tubes are incubated one hour and the tube which contains the least amount of hæmolytic serum and shows complete hæmolysis gives the unit of hæmolysin. Two such units are used in the final test.

e. Red Blood-cells.—At the slaughter house sheep's blood is collected in a wide-mouthed bottle containing glass rods, and at once shaken until the fibrin has separated. At the laboratory the defibrinated blood is washed three times in a centrifuge with sterile salt solution. A 5 per cent. suspension of the cells is made by mixing one part of the washed cells with nineteen parts of salt solution. Such a suspension will keep four or five days. When the salt solution in which the cells are suspended becomes colored with hæmoglobin, a fresh preparation should be made.

In performing the test I have reduced the amount of human serum, complement, antigen and cells to one-half that originally described. The reason for this reduction is that it is possible to obtain sufficient blood for the test from the lobe of the ear, a decided advantage when one wishes to repeat the test frequently. This reduction in reagents has proven satisfactory in about one thousand trials.

My protocol is shown on page 10.

With any method it is important to determine the hæmolytic unit each day, for the hæmolysin may change, and different samples of guinea-pig serum vary slightly as to their complement content. Another advantage in such a determination is that the observer knows the resistance of the red cells for the day. This varies with different samples of blood, and such variations explain why reactions take place more rapidly some days than others. One must always introduce as controls known positive and negative sera, as

well as a tube containing hæmolytic system plus antigen. Only when all controls without antigen, as well as those without positive serum, are hæmolyzed, while the control with positive serum plus antigen is not hæmolyzed, is it safe to make a final report.

Although we may use exactly two units of the hæmolysin in rabbits' serum, that present in many samples of human serum renders the dosage uncertain. Large amounts of hæmolysin will

	Set for diagnosis	Positive control	Negative control	Control of reagents
Control set without antigen	(a) 0.2 c.c. suspected serum.	(a') 0.2 c.c. positive serum.	(a ₂) 0.2 c.c. negative serum.	
	(b) 0.5 c.c. 10 per cent. guinea-pig serum.	(b) 0.5 c.c. 10 per cent. guinea-pig serum.	(b) 0.5 c.c. 10 per cent. guinea-pig serum.	(b) 0.5 c.c. 10 per cent. guinea-pig serum.
Determinative set with antigen	(a) 0.1 c.c. suspected serum.	(a') 0.1 c.c. positive serum.	(a ₂) 0.1 c.c. negative serum.	
	(b) 0.5 c.c. 10 per cent. guinea-pig serum.	(b) 0.5 c.c. 10 per cent. guinea-pig serum.	(b) 0.5 c.c. 10 per cent. guinea-pig serum.	(b) 0.5 c.c. 10 per cent. guinea-pig serum.
	(c) 0.5 c.c. antigen emulsion.	(c) 0.5 c.c. antigen emulsion.	(c) 0.5 c.c. antigen emulsion.	(c) 0.5 c.c. antigen emulsion.

All the tubes are made up to 1.5 c.c. with salt solution, and incubated one hour at 37°C. Add 0.5 c.c. of a 5 per cent. suspension of sheep cells and 2 units of hæmolysin, total volume of all tubes made up to 2.5 c.c. Incubate one and one-half hours or until all controls are hæmolyzed.

mask a partial complement fixation. On this account, I now always introduce an additional control in the Wassermann reaction. This consists of one-half the amount of human serum that is used in the test, plus complement and red cells, but without rabbits' hæmolytic serum. If this tube shows complete hæmolysis, we know that at least two units of hæmolysin are present in the sample of serum, and if the Wassermann reaction happens to be negative, we are justified in repeating the reaction, using the Bauer technic.

Bauer modified the Wassermann reaction by utilizing the hæmolytic power of human serum for sheep cells, thus avoiding the use of rabbits' hæmolytic serum.

In some laboratories this method seems to have given good results, but in this country, at least in New York, the hæmolytic power of human serum for sheep cells is too variable. I have determined this power in 183 sera, only 66 sera, or 31 per cent., contained enough hæmolysin to perform the test.

Hecht goes one step farther, and utilizes both the hæmolysin

and complement present in the human serum. The objection of inconstant antishæp hæmolysin content also holds here. The use of human complement requires active serum. The objections to active serum will be discussed later, while the objections to the use of human complement are given by Noguchi as:

"1. Human complement requires for complete hæmolysis ten times as much amboceptor as an equivalent amount of guinea-pig complement.

"2. Human complement is less sensitive to fixation than that of guinea-pigs.

"3. The quantity of human complement varies greatly, from one to three, with different samples of serum. If it were present in excess it would destroy a positive reaction; hence to be accurate each serum would have to be titrated for complement content before applying the test.

"4. If human complement is used there is no way of telling if antigen alone is anticomplementary.

"5. Old samples of blood cannot be used because complement rapidly deteriorates."

In spite of these objections, M. Stern has employed human complement in a modification of the Hecht technic. To eliminate non-specific reactions she uses a 2.5 per cent. suspension of sheep cells, rabbits' anti-sheep hæmolytic serum in the dose of nine to twelve units, and as antigen one-fifth and two-fifths of the amount of extract that is used in the Wassermann method.

Bruck, who has followed this method with Stern, gives the following conclusions:

1. The serum can be tested after standing several days.
2. This technic has given only specific reactions in 600 trials.
3. With lues sera it is positive in about 15 per cent. more cases than the Wassermann reaction.

A method which has aroused much interest in this country is that of Noguchi. It differs chiefly from the Wassermann technic in using human cells and antihuman hæmolysin instead of sheep cells and anti-sheep hæmolysin. In this way the source of error arising from the hæmolytic power of human serum for sheep cells is eliminated. Other marked differences in technic are that 0.02 c.c. of complement is used to determine the hæmolytic unit, while

double that amount is used in the test. Also, the hæmolysin and antigen are dried on strips of paper. Noguchi claims greater stability for reagents in this form. I have not found that antigen-impregnated papers keep as well as antigen in alcoholic solution. The hæmolytic papers retain their full activity two or three months, but they also deteriorate after a time. Still, while active, they are more convenient than the hæmolysin in fluid form. Lastly, active human serum is used in drop doses. To this active serum I attribute in greater part the sensitiveness of this method. In my work last winter, in which Noguchi's technic was followed as originally described, I obtained thirty-four positive reactions in about two hundred and fifty patients in whom a history of syphilis could be fairly well eliminated. Only three of the thirty-four gave a positive Wassermann reaction.¹ Fourteen were obtained with antigen papers furnished by Dr. Noguchi and twenty with an alcoholic extract of syphilitic liver. These twenty all gave negative Wassermann reactions and also negative Noguchi reactions when the serum was inactivated and used in the same proportion to complement in the latter method as in the former. Further, when these same sera were used in the active state in the Wassermann method they gave positive reactions. For this reason, I concluded that it was not safe to employ active serum in the test for diagnosis. In a study of one hundred and seventy-seven syphilitic sera, it was found that active serum gave slightly better results than inactive with the Noguchi technic, while both were more sensitive than the Wassermann. Noguchi now claims that the non-specific reactions were due to the form of antigen. He has shown that peptones, albumoses, and various cleavage products of bacteria and tissues fix complement when mixed with many active human sera. This fixation is non-specific and disappears when the human serum is inactivated. He claims that the non-specific reactions were due to protein bodies present in the alcoholic extract. These substances are removed by fractionating the evaporated alcoholic extract with ether and acetone. The ether-soluble and acetone-insoluble portion contains nearly pure lipoids, the use of which he claims gives no non-specific reactions with active serum. I think that a comparison

¹ One leprosy, one scarlet fever and one varicella in a child with the stigmata of congenital syphilis.

of total alcoholic extracts with pure lipoids is necessary before we can decide that the latter are as good reagents as total extracts. However, if it is finally shown that some constant chemical method may be obtained for preparing a reagent, the advantage of having a uniform antigen is apparent. Noguchi agrees with me that when total organ extracts are used, the serum to be tested must be inactivated.

Two other reasons may be advanced in favor of inactive serum. First, in some active sera there are substances which exert an anti-complementary action in the control tube without antigen, so that the rule of using in this tube double the dose of serum to be tested cannot be applied. These substances are destroyed in heating to 56° C. In this way we get a pure fixation reaction, and not a summation of anticomplementary action. Second, inactivating destroys human complement and we know more nearly the exact dose of complement present in the test. In comparing active and inactive serum, I have seen weak reactions with the active serum which were strong with the same serum inactivated. Here the weak reaction seemed to be due to the presence of human complement. In such a complicated test it would seem advisable to obtain each factor in as pure a state as possible. Inactivating the human serum gives us the antibody in this condition. The advantage of the Noguchi principle is the accurate dosage of all the other factors. Inactivating, which adds but little to the work involved, gives us a constant method of dosage of human serum, and its uses renders the method as accurate as it is possible to attain when we are dealing with such unstable substances as products of vital processes.

On account of the greater sensitiveness of the active serum method, it seems to me that we shall eventually perform the test with serum in both the active and inactive state. If both are positive we can give a diagnosis of active syphilis if other evidences of the disease are present. If both are negative it is a stronger argument against the presence of the disease than if only inactive serum were used. A positive reaction with active serum alone would demand further investigation, and the ultimate conclusion to be drawn from such a finding, I believe to be still an open question. Kaplan, who used antigen papers prepared by Noguchi, reports 7 per cent. of non-specific reactions with the Noguchi method. Com-

paring this with the Wassermann method, he draws similar conclusions as to the value of the active and inactive serum methods. He thinks both the Wassermann and Noguchi methods should be used in an examination. Similar or more sensitive results may be obtained with less labor and apparatus by using both active and inactive serum.

PRACTICAL APPLICATIONS OF THE REACTION

To be of diagnostic value any serum reaction should be specific for the disease under examination. That the Wassermann reaction is nearly absolutely specific for syphilis is shown by the figures given by Bruck. Among 34 different observers, 5038 cases were examined in which a history of lues could not be obtained. Only 59 of these cases, or 1.1 per cent., gave a positive reaction, and among them a number were strongly suspected of syphilis. When we consider that from 10 per cent. to 40 per cent. of people with late manifestations of syphilis deny infection or secondary symptoms, it is easy to suppose that many of the so-called non-specific reactions are obtained in those who are ignorant of earlier symptoms.

There are, however, certain diseases which have given positive reactions in a high percentage of trials. These are frambœsia, leprosy and scarlet fever. The similarity in symptoms between frambœsia and syphilis, as well as a spirochæta as the etiological agent in each, renders the reactions here of more academic than practical interest, because frambœsia is rarely if ever seen outside the tropics. The serum of animals with trypanosomiasis gives a complement fixation with luetic extracts. This lends support to the theory that the *Spirochæta pallida* is an animal parasite and that the reaction is a group reaction, specific for the lower forms of animal parasites. However, this view is controverted by the findings in leprosy. In this disease various observers report from 10 per cent. to 70 per cent. of positive reactions. The majority of these reactions are obtained in patients with the tubercular form of the disease.

The strongest point against the specificity of the reaction is the large number of positive results obtained in scarlet fever. Fua and Hecht analyze the figures of several observers. In all 353 cases gave 12 per cent. positive reactions. These authors at the same time present 59 cases with no positive reactions. I have collected the

figures presented by various authors in 562 cases (inclusive of the above-named authors), with only 5 per cent. of positive reactions. The positive reactions in scarlet fever do not seriously affect the value of the reaction in syphilis, for in scarlet fever it is transitory, and in positive cases repeated examinations over a period of two months will almost invariably give a final negative reaction, while repeated trials in syphilis will give nearly constant positive reactions. The clinical symptoms of the two diseases are so different that resort to the reaction for differential diagnosis is rarely necessary. Beside the above-mentioned diseases, an occasional case of tuberculosis, carcinoma and malaria have been reported as giving positive reactions. Most of these patients were in a profound cachectic state.

THE REACTION IN THE VARIOUS STAGES OF SYPHILIS.—Primary Stage.—Here the percentage of positive reactions varies more than in any other active stage. This is no doubt due to the different periods at which the tests are made. Different reports vary between 70 per cent. and 100 per cent., with an average of 80 per cent. of positive reactions. The frequency of positive reactions increases as we near the secondary stage, and is found in over 80 per cent. of cases in the sixth week after infection.

The earliest case to give a reaction is reported by F. Lesser. The blood was examined and found positive eight days after exposure. Fourteen days later an initial lesion appeared, with six weeks later a typical roseola. According to the observations of Neisser on apes, a positive reaction is an indication of a general invasion of the body by the syphilitic virus. After an infected ape gave a positive reaction, its skin resisted reinfection.

In repeated examination of patients in the primary stage, we sometimes see a negative reaction followed, in a few days, by a positive one. With such findings the diagnosis is nearly absolute. The Wassermann reaction is not found as early as the *Spirochæta pallida*. This is specially true in genital lesions, but in lesions about the mouth other non-pathogenic spirochætæ render a positive *Spirochæta pallida* diagnosis less certain. In such instances, the serum reaction has more relative value. We also see initial lesions nearly healed, and some that are herpetic in nature where spirochætæ cannot be demonstrated. When such lesions are present, the

reaction is of the greatest value. It has been suggested that if *Spirochæta pallida* is demonstrated in an initial lesion, the lesion be excised and energetic treatment instituted. If the reaction never becomes positive the prognosis is better than if secondary symptoms have been awaited.

Secondary Syphilis.—According to different observers a positive reaction is found in from 90 per cent. to 100 per cent. of untreated cases. If we re-examine the negative cases with a more sensitive extract a number of them are positive. A few of the negative reactions are due to a high anti-sheep hæmolysin content, and if these sera are examined with the Noguchi modification, they are found to be positive. As with all other biological reactions, a similar response to the virus does not take place in all individuals, so that a negative reaction does not absolutely eliminate syphilis, but repeated, properly controlled negative reactions speak strongly against the presence of the disease. In a majority of the cases of secondary syphilis the eruption is so typical that resort to the reaction for diagnosis is unnecessary, but it is well to know the strength of the reaction during this stage, so that we may have some criterion with which to judge the effect of treatment in later years. In a few cases in which the roseola has been masked by other eruptions, such as scabies, the diagnosis of syphilis has been confirmed by the reaction.

Tertiary Syphilis.—Here the figures vary more than in the secondary stage. From 60 per cent. to 100 per cent. of positive reactions are reported by various observers, with an average of 80 per cent. The reason for the variation is two-fold: First, many of the cases have been under considerable treatment which has a marked effect on the reaction. Second, the virus is more localized and the spirochætæ fewer in numbers than in the secondary stage. This diminution probably gives a weaker stimulus to the production of antibodies. In this stage the reaction has more diagnostic value, for many of the visible forms of late syphilis closely resemble the other infectious granulomata, and all diagnostic aids must be invoked before a positive opinion can be expressed.

The relation of leukoplakia to syphilis has been elucidated more fully by the reaction. It has been shown that about 90 per cent. of patients with leucoplakias give a positive reaction, and in

Neisser's clinic all of the positively-reacting cases improved under energetic syphilitic treatment.

Latent Syphilis.—It is in the so-called latent stage of lues that the reaction throws much light on the status of the disease. It is found positive in from 40 per cent. to 70 per cent. of cases of latency depending on the time since infection, number of relapses, amount and efficiency of medication and time since last treatment. In all about 50 per cent. give a positive reaction. Taking up the study by years we find it in the first two years in 70 per cent. of cases; from the third to the thirtieth in 50 per cent.; from the thirtieth to the thirty-fifth year after infection in 11 per cent., and only exceptionally after the thirty-fifth year. Lesser, who gives the figures above quoted, calls attention to the striking similarity between findings in the serum reaction and the results of the autopsy room. In over four years' autopsy experience in Berlin he found evidence of visceral syphilis in 49 per cent. of subjects in whom a previous history of lues could be obtained. With the serum reaction 46 per cent. of all latent cases were positive. These figures so nearly correspond that it is quite suggestive that latency may mean only that the disease is not in evidence on the surface and is not giving clinical symptoms, but is still active in some of the more vital organs. Indeed, Citron states that a case should not be considered latent so long as the reaction persists. His reasons for such a contention are: First, the constant finding of the reaction in manifest lues. Second, the fact that untreated or poorly treated individuals show the reaction after many years. Other bacterial antibodies begin to diminish in a week to a month after the disease has ceased being active. If the lues reaction is present after ten years or more it must be due to the fact that there is a constant production of antibody, brought about by the presence of the specific organism in the system. Third, cases which have no other symptoms, but show a positive Wassermann reaction, lose the reaction under mercurial treatment. This shows that through the specific therapy toxic substances are removed, the formation of reagin stops, and the reaction becomes gradually weaker. He claims that we should consider the reaction a symptom and so long as any symptom persists the process is not latent. Where the line shall be drawn between latent syphilis in the light of modern study is a hard question to decide.

In syphilitic diseases of the various viscera the reaction is of great value to the internist, while scarcely a specialty exists in which the results of the reaction have not proven that it is of great value.

The reaction has thrown much light on the so-called para-syphilitic diseases. Lesser's figures show that 100 per cent. of cases with general paralysis give a positive result. Marie and Lévaditi, in studying the spinal fluids in this condition, found that in the incipency of the disease there were a much smaller number of positive reactions than later when the paralytic symptoms had progressed and the patients were in a stage of dissolution. In these studies the percentage of positive findings was in direct proportion to the activity of the morbid process. Lesser's findings clearly indicate the relation of syphilis to tabes. While he obtained a positive serum reaction in only 34 out of 61 cases examined, 45 of the cases, or 74 per cent., gave a previous history of syphilis. Of the remaining sixteen who denied infection, thirteen gave a positive Wassermann reaction. One of the remaining cases gave a history of injury as the etiological factor. Of the whole number 58, or 95 per cent., were directly proven to have had syphilis.

Congenital Syphilis.—In no other manifestation of syphilis is a positive reaction so constant. In children with symptoms a positive reaction is found in practically every trial. Over 70 per cent. of apparently healthy mothers giving birth to syphilitic children show a positive reaction, and about the same percentage of apparently sound children from mothers with symptoms of syphilis give a reaction. If we accept the view that positive reactions without other symptoms denote latency we see that the periods of immunity defined by Colles's and Profeta's laws are really periods of latency. In institutions where wet nurses are furnished, the reaction has shown that about 10 per cent. of such women are syphilitic, and in the light of modern knowledge it is advisable never to accept a wet nurse without trying the reaction. If there is any suspicious rash a test should also be made on the child, so that both the nurse and child may be spared the possibility of contracting the disease, the one from the other.

The Reaction as a Guide to Treatment.—Important as is the reaction from the standpoint of diagnosis, its application has

rendered it necessary for us to revise our views of the treatment of the disease. The effect of specific treatment on the reaction was noted from the time of the earliest observations. Many reports have been made on this point. A few typical figures are cited below:

Citron—treated, 65 per cent. positive; untreated, 81 per cent. positive.

Bruck—treated, 29 per cent. positive; untreated, 82 per cent. positive.

Bering—well treated, 16 per cent. positive; untreated or poorly treated, 75 per cent. positive.

Ledermann—latent lues, untreated, 81 per cent. positive; one to three courses of treatment, 73.9 per cent. positive; four or more courses, 47.7 per cent. positive.

The results of Jesionek and Mierowsky give a beautiful example of the effect of treatment in latent lues:

Number of courses..	0	1	2	3	4 and 5	6 and 7	8 and more
Number of cases ...	76	85	76	55	76	38	16
Per cent. positive ..	97.3	64.7	50	47.3	42.1	34.2	31.2

Citron, from observing the intensity of the reaction in relation to treatment, has formulated the following laws:

1. The longer the syphilitic virus has worked in the body and the oftener it has caused relapses, the more constant and stronger is the antibody content of the serum.

2. The earlier the mercurial treatment is begun, the longer it is continued, the more often it is repeated, and the more efficient the manner of application, the lower is the antibody content.

Injectations and inunctions seem to have a more rapid effect on the reaction than mercury given by the mouth. The reaction has also been observed to disappear under iodides, atoxyl and arsenophenylglycin.

These observations all lead to the conclusion that the reaction should be an important guide in treatment.

1. As soon as a positive reaction appears in primary syphilis, treatment should be instituted. The reaction, with the presence of *Spirochaeta pallida* renders a diagnosis positive, and by starting

treatment before the appearance of secondary symptoms a dangerous saturation with the virus will frequently be avoided, and the danger of the patient becoming an active distributor of the spirochætæ minimized.

2. In the first three years of the disease treatment can be more rationally controlled, than by merely following the rule of a certain amount of treatment, with periods of rest. By means of frequent observations, in many cases the disease can be controlled with a small amount of mercury, while others will require constant application to treatment.

3. In the late latent period a positive reaction is an indication for further treatment, and, as a rule, treatment should be continued until the reaction becomes negative. This rule should, of course, be modified according to the condition of the patient. If he tolerates mercury badly, or presents other contraindications to treatment, the indications for the individual case must be recognized and met. Perhaps some reactions will never yield, but it is in such cases that the prognosis is probably bad, and such patients that we may expect to go on to tabes or general paralysis. A persistent negative reaction is a good prognostic sign; a returning reaction is a warning that a relapse may be imminent, and is sufficient indication for renewed treatment. In former times the treatment of syphilis was guesswork founded alone on clinical symptoms. The Wassermann reaction is one of the most reliable guides both to diagnosis and treatment that has ever been given to the medical world. If we will regard it as a symptom of the disease, and use it as we would any other symptom, we shall have a proper idea of its importance.

REFERENCES

- BAUER, J.: *Deutsch. med. Wchnschr.*, 1908, xxxiv, 698.
BERING, F.: *München. med. Wchnschr.*, 1908, lv, 2476.
BORDET and GENGOU: *Ann. d. l. Inst. Past.*, 1901, xxv, 288.
BRUCK, C.: *Die Serodiagnose der Syphilis*, Berlin, 1909.
CITEON: *Handbuch d. Immunitätsfor.* (Kraus and Lévaditi), vol. ii.
ELIAS, PORGES, NEUBAUER and SALOMEN: *Wien. klin. Wchnschr.*, 1908, xxi, 376.
FUA and HECHT: *Wien. klin. Wchnschr.*, 1909, xxii.
GAY, F.: *Centralbl. f. Bact.*, 1905, xxxix, 603.
HECHT, H.: *Wien. klin. Wchnschr.*, 1908, xxi, 1742.
JESIONEK and MIEROWSKY: *München. med. Wchnschr.*, 1909, lvi, 2297.
KAPLAN: *Am. J. M. Sc.*, 1910, No. 1.

- KRAUS and VOLK: *Wien. klin. Wchnschr.*, 1906, xix, No. 21.
 LEDERMAN, K.: *Med. Klin.*, 1909, v, 419.
 LESSER, F.: *Deutsch. med. Wchnschr.*, 1909, xxxiv, 379.
 LIEFMANN, H.: *München. med. Wchnschr.*, 1909, lvi, 2097.
 MICHAELIS, L., and LESSER, F.: *Berl. klin. Wchnschr.*, 1908, xiv, 301.
 NOGUCHI, H.: *Proc. Soc. Exper. Med. and Biol.*, 1909, vi, 77; *J. Exper. M.*,
 1909, xi, 392; *J. Am. M. Ass.*, 1909, liii, 1532; *Proc. Soc. Exper. Med.*
and Biol., 1909, vii, No. 2.
 SACHS H.: *Semaine méd.*, 1908, xxviii, 301.
 STERN, M.: *Zeitschr. f. Immunitätsfor.*, 1909, i.
 SWIFT, H. F.: *Arch. Int. Med.*, 1909, iv, 376, 1494.
 WASSERMANN, A., and BRUCK, C.: *Med. Klin.*, 1905, i, 409.
 WASSERMANN, A., NEISSER, A., and BRUCK, C.: *Deutsch. med. Wchnschr.*, 1906,
 xxxii, 755.

FURTHER STUDIES ON THE SERUM DIAGNOSIS OF SYPHILIS WITH ESPECIAL REFERENCE TO THE ANTI HUMAN HÆMOLYTIC SYSTEM

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REMARKS ON TECHNIC

Soon after the first publication of my system of serum diagnosis of syphilis¹ a few improvements in minor technical points were added and the method as it has been used since February 1909, may be very briefly described below. For details of methods of preparation, titration, etc., for a practical working basis the reader is referred to my monograph² which has just appeared.

Complement.—Fresh serum of guinea-pig in strength of two units,³ usually 0.1 c.c. of a 40 per cent. dilution of the serum for each tube. According to the activity of a given specimen of complement-containing serum the quantity may be somewhat greater or less, and this is subject to a preliminary titration. It is best to use the serum after it has been kept in contact with the clot overnight in a refrigerator, and, if possible, to use a mixture of more than two sera from different guinea-pigs in order to obtain uniform results, because guinea-pig's complement, while fresh and normally reactivating for the amboceptor sometimes shows variations in fixation quality. Some sera may be highly refractory to fixation, thus giving a fallacious negative reaction with a positive syphilitic serum. Dried complement offers no advantage, is difficult to prepare, liable to lose its activity suddenly, and it is not to be recommended.

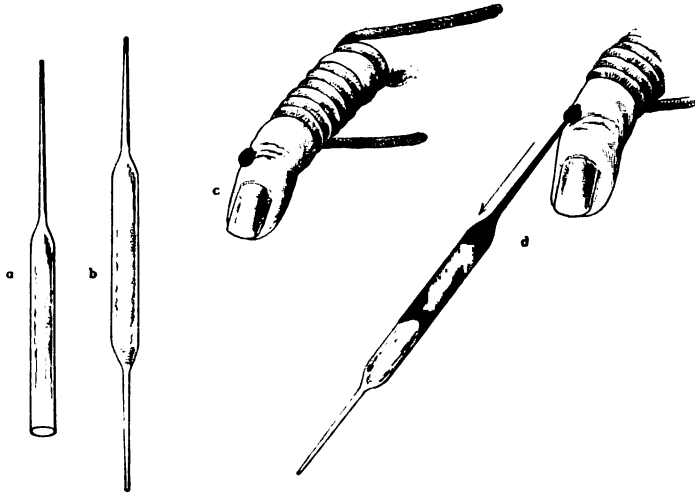
AMBOCEPTOR.—Serum from rabbits sufficiently immunized by

¹ Noguchi: A new and simple method of serum diagnosis of syphilis, Jour. Exper. Med., 1909, xi, 392.

² Noguchi: Serum Diagnosis of Syphilis, J. B. Lippincott Company, Philadelphia, 1910.

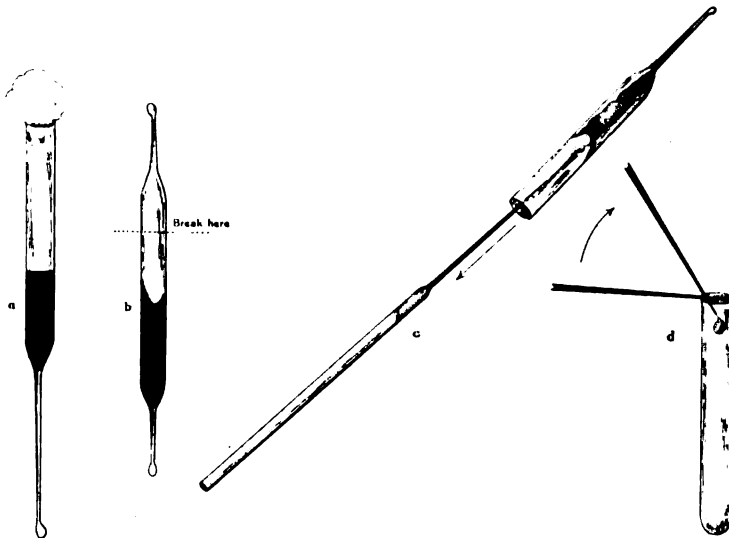
³ One cubic centimetre of one per cent. suspension of washed human corpuscles and one unit of antihuman amboceptor are used to determine the unit of complement here mentioned. In the test two units are used.

FIG. 1.



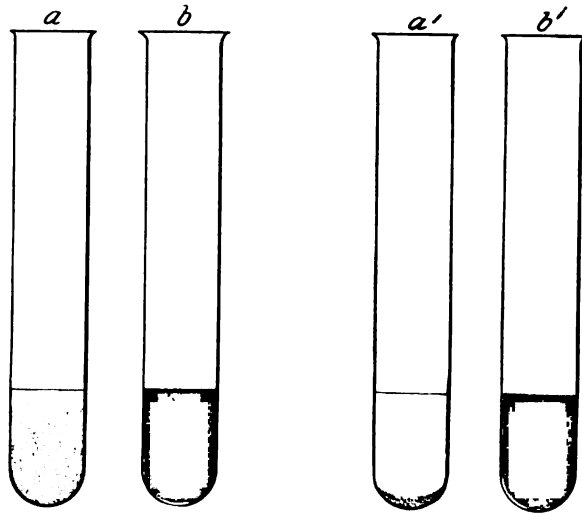
a, blood-collecting tube; b, the same for transportation (both ends can be sealed); c and d show a simple method of collecting the blood from an adult.

FIG. 2.



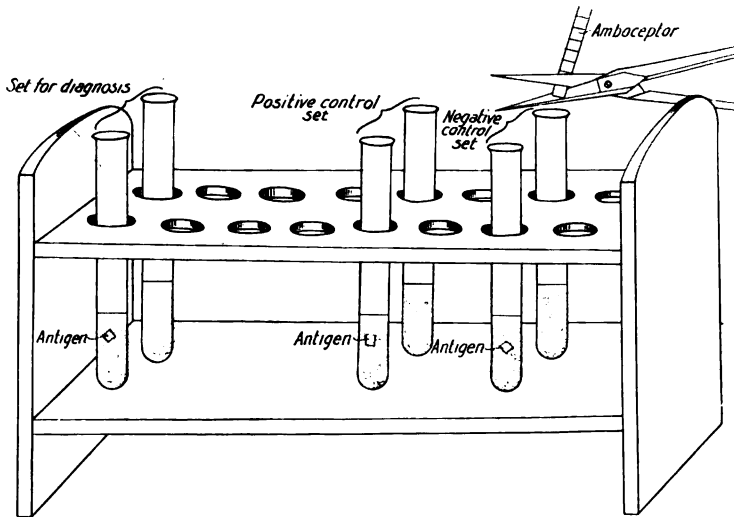
a and b show two blood-collecting tubes with specimens of blood. The clot is retracted from the wall and the space around it is filled with clear serum. c and d show steps for taking out the serum and placing it in a haemolytic test-tube by means of a capillary pipette.

FIG. 3.



a, suspension of red corpuscles shaken up with salt solution; *b*, hæmolysis of the corpuscles, the hæmoglobin being diffused through the fluid. On standing, the intact corpuscles settle to the bottom (*a'*), the hæmoglobin in solution shows no change (*b'*).

FIG. 4.



The picture shows the appearance of all tubes after the first incubation and just at the moment when the amboceptor slip is about to be added. Thus far there is no visible difference in these tubes and the corpuscles are still intact. In all front tubes there are small square pieces of paper representing the antigen; none in the rear tubes. The controls *without antigen* show that hæmolysis will not be prevented by any constituent of either syphilitic or non-syphilitic serum; the negative control *with antigen* shows that the antigen itself does not have the power of inhibiting hæmolysis. The positive control *with antigen* shows that there is no unknown factor present to interfere with the deviation of complement.

several successive injections of washed human corpuscles.⁴ The serum is inactivated before use. It may be used in liquid or in dried paper form. The latter is much more stable and excludes a possible bacterial contamination. No appreciable weakening takes place in any climates when kept perfectly dry. The titration of dried amboceptor paper can be carried out just as accurately as with the liquid amboceptor. For the fixation test two units of amboceptor are used for each tube. The liquid preparation is diluted to such a strength that 0.1 c.c. contains two units of amboceptor. With the paper amboceptor it is convenient to have two units in about 5 mm. x 5 mm.

*Corpuscle Suspension.**—One cubic centimetre of a 1 per cent. suspension of washed human corpuscles is used for each tube. Any non-syphilitic individual or the patient himself can furnish the blood for preparing the suspension. Removal of serum from the corpuscles by means of centrifugalization or sedimentation is necessary. It is understood that the corpuscles of the patient are to be used only with his own serum. Use fresh corpuscles always.

Patient's Serum.†—In my system it can be used in two different states, namely, unheated (active) or heated (inactivated). Active and inactivated sera give the same results when properly used. It is important not to use aqueous or alcoholic extracts of syphilitic liver as antigen with active sera, because certain ingredients, proteins, glycogen, etc., contained in these preparations cause occasional non-specific complement fixation⁵ with unheated human sera. In order to avoid this, the acetone-insoluble fraction of tissue lipoids free from these substances is used. When examining inactivated sera this precaution is unnecessary, as non-specific fixation does not occur after inactivation. The quantity of active serum for each tube is 0.02 c.c., and that of inactivated serum 0.08 c.c.⁶ For routine work a capillary pipette with suitable

* Must be washed thoroughly. (See Noguchi; "The Fate of so-called syphilis antibody in the specific precipitation reaction," Proc. Soc. Exper. Biol. and Med., 1909, vii, 16.)

* Noguchi: On non-specific complement fixation, Proc. Soc. Exper. Biol. and Med., 1909, vii, 14.

* Noguchi: A simple and rational serum diagnosis of syphilis, Jour. Amer. Med. Ass., 1909, liii, 1532.

* See Fig. 3.

† See Figs. 1 and 2.

calibre is sufficiently accurate for measuring the serum. The quantity of cerebrospinal fluid is 0.2 c.c. for each tube.

Antigen.—As stated above, only the acetone-insoluble fraction of tissue lipoids should be employed for active sera. With inactivated sera no such precaution is necessary as long as a given antigen preparation is suitable. The acetone-insoluble fraction can be used in liquid or dried paper form. The dose of antigen is titrated by the experimenter before assigning quantities.

Performance of the Test.—In making the test do not omit any necessary control under any circumstance. Positive syphilitic serum, normal serum and the plain hæmolytic system, each set with and without antigen, must be included in every series of tests. Chart I (p. 25) represents the complete procedure, Figs. 5 and 6 showing the appearance of the tubes of the test set, positive control, and negative control.

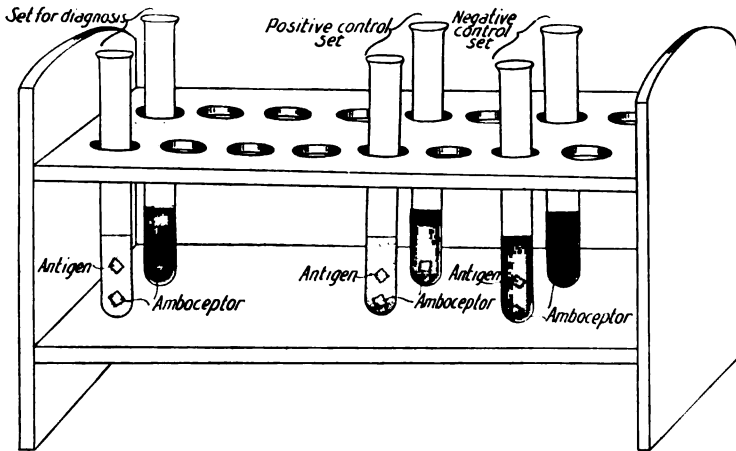
I usually add the corpuscle suspension to the mixture at the beginning, but it may be added after the first incubation at the same time as the amboceptor, in the regular Wassermann system.* In this case 1 c.c. of 0.9 per cent. salt solution instead of 1 per cent. corpuscle suspension is added to the first factors (serum, complement, antigen). At the end of the first incubation 0.1 c.c. of 10 per cent. suspension of washed corpuscles is added, together with two units of amboceptor. It is immaterial which way one proceeds. The second incubation is for two hours at 37° C., then after a few hours at room temperature the final results are read.

PRACTICAL RESULTS

Since the introduction early in 1909 my system has been tried in over 8500 cases by different investigators. It has been compared with the original Wassermann system in 1993 cases of syphilis and parasyphilis. Besides, 1488 cases belonging to the above group of diseases were examined by this system with the clinical controls alone. In regard to non-syphilitic cases it has been tried on 3296 cases, including scarlet fever, leprosy, malignant tumors, yaws, tuberculosis, etc., which have been reported to give occasional positive reactions with the Wassermann system. The method has also been applied to about 1400 miscellaneous cases for diagnosis, and to 550 cases, including various conditions of the eye (with Dr.

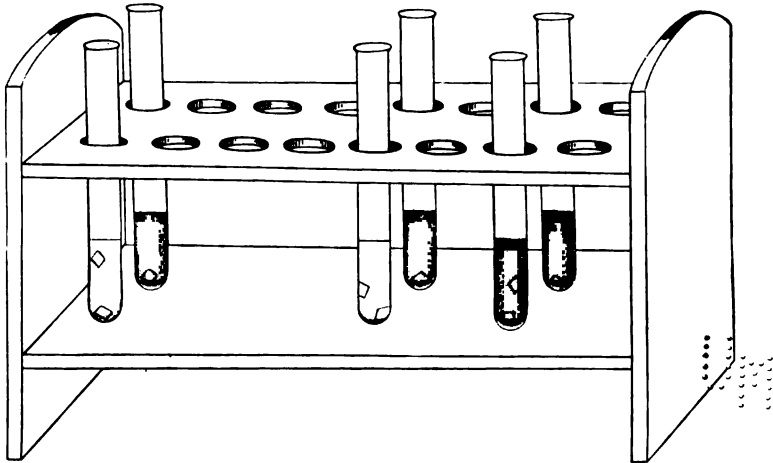
* See Fig. 4.

FIG. 5.



This picture shows the appearance of the tubes after completion of hæmolysis, namely, after the second incubation of the same tubes as shown in Fig. 4 with addition of antihuman amboceptor slips. In all front tubes there are two square pieces of paper, one representing antigen and the other amboceptor. In each rear tube there is but one piece, and it represents amboceptor. In negative control set hæmolysis occurred in both tubes. In positive control set hæmolysis took place in the rear tube only and not in the front. In the set for diagnosis the conditions are seen to be identical with the positive control set, hence this serum is found to be syphilitic.

FIG. 6.



This picture shows the appearance of the tubes shown in Fig. 5 after standing for several hours. The absence of hæmolysis in the front tubes of positive control and diagnostic sets is shown by clear supernatant salt solution over the deposited intact corpuscles. The absence of hæmolysis means positive reaction in these instances. These tubes show that in the absence of the specific hæmolytic amboceptor hæmolysis will not be caused by any ingredient of the other reagents or their compounds. In such of the tubes of the front row as contain syphilitic antibody the complement has been deviated, and no hæmolysis can be produced later by adding hæmolytic amboceptor.



CHART I.

Serum to be tested.	Positive control.	Negative control.	Hæmolytic system control.
<p>Patient's serum 0.02 c.c. (when inactivated, 0.08 c.c.) Complement (40%) 0.1 c.c. Corpuscle suspension (1%) 1 c.c.</p>	<p>Positive syph. serum 0.02 c.c. (when inactivated, 0.08 c.c.) Complement (40%) 0.1 c.c. Corpuscle suspension (1%) 1 c.c.</p>	<p>Normal serum 0.02 c.c. (when inactivated, 0.08 c.c.) Complement (40%) 0.1 c.c. Corpuscle suspension (1%) 1 c.c.</p>	<p>No serum. Complement (40%) 0.1 c.c. Corpuscle suspension (1%) 1 c.c.</p>
Front	Rear		
Same as above with antigen.	Same as above with antigen.	Same as above with antigen.	Same as above with antigen.
Incubated at 37° C. for one hour, then two units of amboceptor added.			
Second incubation at 37° C. for two hours. Tubes frequently shaken at the beginning.			

Remarks: The quantity of complement is subject to variation according to the activity of the serum. In my monograph the quantity of complement is expressed in terms of undiluted serum, hence it is given as 0.04 c.c., which is equivalent to 0.1 c.c. of a 40 per cent. dilution. One must not be confused on this point.

Cohen), ear (with Dr. Fowler), and in backward children (with Dr. Atwood).

In Tables I and II the results obtained by different workers in cases of syphilis and parasyphilis are presented.

From the tables it is evident that my system gives a somewhat higher percentage of positive reactions than the original Wassermann system. That this superior delicacy of the reaction does not depend upon an *undue* sensitiveness of the system has been repeatedly pointed out.⁷ Any one who understands the disturbing effect of an excessive amount of amboceptor in a complement fixation test ought to have no difficulty in finding out that this is the reason for the difference in results between the two systems.

The antihuman system has been tested in a very large number of non-syphilitic cases. While the number of controls is increasing gradually as time passes, I am already in possession of several reports from various investigators who have been using this system at different hospitals and laboratories. The results are briefly mentioned below.

Noguchi, ¹ 1142.	Craig, ¹⁴ 162.
Kaliski, ⁸ 550	Corson-White, ¹⁵ 183.
Jefferies ⁹ and Pease, ¹⁰ 300.	Fox, ¹⁶ 113.
Schwarz (B), ¹¹ 300.	Groat, ¹⁷ 51.
Daisy Robinson, ¹² 200.	Potter (Alfred), ¹⁸ 45.
Lederer, ¹³ 150.	Schradieck, ¹⁹ 100.
Total number, 3296.	

¹ Noguchi: Some critical considerations on the serum diagnosis of syphilis, Proc. Soc. Exper. Biol. and Med., 1909, vi, 77.

⁸ Pathological Laboratory, Mount Sinai Hospital, New York.

⁹ Pathological Laboratory, New York Polyclinic Medical School.

¹⁰ Post-graduate Medical College, New York.

¹¹ Pathological Departments of the Bellevue Hospital and of the Gouveneur Hospital, New York.

¹² Dermatological Clinics of the New York Polyclinic Medical School and of the Northwestern Clinic.

¹³ Pathological Laboratory of the Jewish Hospital, Brooklyn.

¹⁴ U. S. Army Medical College, Washington, D. C.

¹⁵ Department of Neuropathology, University of Pennsylvania.

¹⁶ Dermatological Department of the New York Skin and Cancer Hospital.

¹⁷ Department of Chemical and Microscopical Diagnosis, College of Medicine, University of Syracuse.

¹⁸ Pathological Laboratory of the Long Island State Hospital, New York.

¹⁹ Dermatological Department of the Long Island Medical College, New York.

TABLE I.

	Primary syphilis			Secondary syphilis			Tertiary syphilis			Latent syphilis			Congenital syphilis			Cerebrospinal syphilis			Total
	No. of cases	W.	N.	No. of cases	W.	N.	No. of cases	W.	N.	No. of cases	W.	N.	No. of cases	W.	N.		P. ct.		
Noguchi	23	73.9	86.9	79	87.3	96.2	65	80	87.6	59	61	75.5	4	100	100	100	5	80	235
Noguchi	70	92.8	197	37	97	100	177	89.9	270	46	74.4	17	100	100	100	100	100	731	131
Fox	7	100	100	37	97	100	32	71	84	54	62	1	100	100	100	100	100	709	709
Kaplan	138	90	97	281	86	98	191	73	81	79	51	75	20	90	90	90	35	80	226
Swift	16	81	81	76	92	97	45	80	88	85	55	62	4	100	100	100	100	80	309
Corson-White	14	86	100	146	98	99	47	80	80	28	60	64	39	100	100	100	100	119	309
Craig	37	51*	50	50	78	78	16	68.7	12	83.3	4	4	4	75	75	75	15	75	182
Potter (Alfred)	7	86	86	71	98.6	46	78	66	66	11†	2	100	100	100	100	100	1	100	50
Groat	9	100	100	24	89	89	5	60	88	9	66	66	4	75	75	75	34	34	34
Berghausen	5	100	100	15	93	93	9	74	74	6	101	6	100	100	100	100	15	75	101
Kalski	326	86	93	1001	92	95	683	77	80	660	55	63	101	93	94	56	80	84	2827
Total																			

* Includes very early cases. † The majority under treatment.

TABLE II.

	General paralysis						Tabes					
	Blood serum			Cerebrospinal fluid			Blood serum					
	Number of cases	W.	N.	Number of cases	W.	N.	Number of cases	W.	N.			
Noguchi	25	..	86	86	125	..	68			
Rosanoft and Wiseman ..	56	..	80	44	..	86	8	44	72			
Kaplan	61	65	72	86	205	60	65			
Swift	3	67	100	5	100	100	3	100	100			
Corson-White	11	80	80	100	38	55	68			
Groat	2	100	100	100	49	70	75			
Kalski	3	100	100	100	6	..	66			
Total	161	71	88	49	100	93	444	66	73			

Detailed accounts of the cases above quoted will be found in the reports of individual investigators. Suffice to say that the varieties of diseases studied by these workers cover every branch of medicine. Some investigators examined the specimens from patients in the wards, going from bed to bed, without reference to the clinical history until the tests were finished. Others examined specimens from patients who have been under close observation for many years and in whom syphilis could be definitely excluded. Still others examined certain special groups, such as dermatological, ophthalmological, neurological, psychiatric, or otological, cases. So far as the results of the above cited investigators are concerned there was no positive reaction in non-syphilitic cases, except in some cases of leprosy, yaws and in 3 out of several hundred cases of malignant tumors. Tuberculosis did not give a positive reaction in a large number examined. Craig observed two positive reactions in cases of malaria at the febrile climax. The reaction was absent during the afebrile period. In regard to scarlet fever, I examined 63 cases and obtained one strongly positive reaction and two slight inhibitions. The strongly positive one was afterwards proven to be a case of congenital syphilis by the accidental infection of two surgeons in charge. Thirty cases of pellagra were studied by Fox with negative results.²⁰ Craig obtained similar results in 8 cases of the same disease. In leprosy I obtained 7 positive reactions in 10 cases. Fox examined 60 cases of leprosy and reports 28 positive reactions in 38 cases of tubercular and mixed types, and 3 positive out of 22 cases of maculo-anæsthetic type. Potter reports two positive results in tuberculous leprosy and one negative in the anæsthetic type. Nichols obtained a weak positive reaction in his yaws patient.

The investigators used active human sera with acetone-insoluble lipoidal antigen in obtaining these results.

It is now too well known to be repeated here that the original Wassermann system also gives positive reactions in leprosy, yaws, certain cases of malignant tumors, and malaria.

Against the findings of the above investigators Swift reported 35 positive reactions (!) in 201 cases of non-syphilitic diseases by using active sera in my system. This difficulty is said to disappear after inactivation of the sera to be tested. It was unfortunate that Swift did not use the acetone-insoluble fraction of

²⁰ Fox: The Wassermann Reaction (Noguchi's modification) in Pellagra, N. Y. Med. Jour., 1909, December 18.

tissue lipoids as antigen; he employed an alcoholic extract of the liver of a congenitally syphilitic fœtus prepared by Michaelis and Lesser's method. This deviation from my usual technic might have been the cause of this disastrous result.^{21 22}

Kaplan once reported 8 per cent. positive reactions in non-syphilitic cases. This investigator informs me now that he has not been having such non-specific reactions by my system during the past five months. His early statistics, including the results obtained during the first few months of his work, are declared inaccurate by him.

With my co-operation Rosanoff and Wiseman examined the sera of 334 cases of non-parasyphilitic psychoses and the cerebrospinal fluids of 243 cases among the same group of patients. The

²¹ Swift: The use of active and inactive serum in the complement deviation test for syphilis, *Arch. Inter. Med.*, 1909, iv, 494; A comparative study of serum diagnosis in syphilis, *Op. cit.*, 1909, iv, 376.

²² Through the courtesy of Dr. W. T. Longcope, Director of the Ayer Clinical Laboratory of Pennsylvania Hospital, Philadelphia, on January 12, 1910, I was given an opportunity to demonstrate whether my modified method of the Wassermann reaction gives positive reaction in non-syphilitic cases, as was reported by Swift, who had reported 35 positive reactions in 201 non-syphilitic cases, using active serum for my test. In the presence of Dr. Longcope and his associates, Drs. Draper, Krumbhaar, and Steinke, and Dr. White, of the University of Pennsylvania, Dr. Swift and I made the following comparative tests, Dr. Swift using the original Wassermann method, while I employed my own method. In all 59 cases were examined by my method, with the following results:

NO HISTORY OR SYMPTOMS OF SYPHILIS

Chronic colitis	1 neg.	Syphilis (second-ary)	1 strong posit.
Otitis media	1 neg.	Cerebral syphilis (inject'n of Hg.)	1 negative.
Chronic bronchitis	1 neg.		
Hernia	2 neg.		
Abscesses	3 neg.	General paralysis..	5
		Serum 4	2 strong posit.
			2 negative.
		Spinal fluid	1 strong posit.
Rheumatism	9 neg.		
Hemorrhoid	1 neg.		
Broken arm	1 neg.		
Necrosis of foot	1 neg.		
Appendicitis	1 neg.		

finding was positive in 45 sera and in 12 spinal fluids. Syphilis was ascertained in 15 cases. Corson-White found 15 positive reactions in 111 neurological cases, 8 of which were in 24 cases of epilepsy. Her examinations were done not only by my system, but also by the Wassermann system, and the results obtained were the same. Rosanoff and Wiseman obtained many positive reactions in dementia præcox (15 in 131 cases) and epilepsy (12 in 69 cases). These results are in harmony with those of Raviart, Breton, Petit, and Levaditi and Raubinovitch who used the original method on their patients. With my co-operation an analysis of

Cardiorenal	4 negative.
Lateral sclerosis	1 negative.
Hemoplegia	4 negative.
Mitral and aortic	1 negative.
Typhoid	8 negative.
Pleurisy	1 negative.
Polyserositis	1 negative.
Pneumonia	6 negative.
Jaundice	1 negative.
Gastric ulcer	1 negative.
For diagnosis	1 negative.
Tertiary syphilis (?)	1 negative.

Dr. Swift was limited to the same five cases of general paralysis and one positive syphilitic case as above, and he obtained exactly the same results, namely, two positive out of four, with the sera of general paralysis, one positive using the spinal fluid, and one positive using the syphilitic serum.

Special mention must be made of the fact that none of the sera examined showed any appreciable anticomplementary property when used in the active state. There is no ground for attributing to my antigen my failure to obtain positive reactions because my results and the results obtained by Dr. Swift with his antigen, which he states had been employed with satisfaction, were identical. My antigen had previously been tested to the satisfaction of all clinicians who had sent me specimens.

In giving instructions at present, I make it a rule that the non-syphilitic cases be tested first in order that such results as reported by Swift may not be obtained. It is understood that while studying these non-syphilitic cases, controls with several positive sera accompany the test in order that the degrees of positive reaction may be studied.

It is my conviction that as long as one uses protein-free lipid antigen, he will never obtain positive reaction with active human sera unless the specimen comes from a syphilis, leprosy or yaws patient.

In conclusion, I may say that this demonstration in 59 cases should be considered decisive because it was done in the presence of many laboratory workers and by the person criticised.

over 200 imbecile children has been made by Atwood, who will report the findings in detail.

The results obtained by Cohen on 200 ophthalmological cases and by Fowler on 127 otological cases, and by Robinson on 200 dermatological cases should be of interest to the corresponding specialists. They all agree with the clinical evidences.

It is hoped that the presentation of the above facts may be useful to many who are interested in the serum diagnosis of syphilis.

THE NEWER DIAGNOSTIC METHODS OF SYPHILIS OF THE NERVOUS SYSTEM*

BY B. SACHS, M.D.

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To appreciate the good results obtained by recent diagnostic methods in relation to syphilis of the nervous system, it is only necessary to recall the vague manner in which, only a few years ago, we decided whether or not any one of a half a dozen organic diseases of the central nervous system was due to syphilis. The clinical symptoms were often entirely identical with those due to other forms of organic disease. We were proud of the fact that we could be independent of the history given by the patient, and could recognize by certain groupings of symptoms that the disease was due to an antecedent syphilitic infection. There were certain earmarks about the hemiplegias, the chronic forms of meningitis, and the various forms of myelitis which were thought peculiar to syphilitic disease and not to other forms of cerebral or spinal affections, and when the clinical expression of disease left us in doubt we were content to accept the luetic origin if the pupils were immobile, if the contours were irregular, if the patient had frequent nocturnal headaches, if he had had hemiplegic attacks from which he recovered, if the symptoms were asymmetrically developed, or if the disease showed unusual remissions and exacerbations. We may now confess that we often made fortunate guesses.

Nowadays the procedure is a very different one. In hospital and in private practice if the question comes up of the luetic origin of a cerebral or spinal affection we take recourse to an examination of the cerebrospinal fluid or attempt the Wassermann reaction of the blood and of the fluid obtained by lumbar puncture. It is to the credit of French neurologists that they were the first to point

* Read by invitation before the Philadelphia County Medical Society, January 12, 1910.

out the value of an examination of the cerebrospinal fluid in the early forms of tabes. Sicard, Nageotte, Widal, *et al.*, were the first to show that an increase of cellular elements, a lymphocytosis, was characteristic of the fluid obtained from patients suffering from tabes and general paresis. In more than 90 per cent. they discovered a very considerable lymphocytosis. German neurologists then took up the subject, and Erb, of Heidelberg, together with his assistant, Schoenborn, were the first in that country to publish a corroboration of French investigations. It was a little disconcerting that Merzbacher, Nissl, and others, while corroborating the findings in tabes and general paresis, found similar changes in persons who had passed through a luetic infection but did not exhibit the symptoms of these two well-known diseases. A moderate lymphocytosis, it was claimed, was found in cases of tumor of the central nervous system, in idiopathic epilepsy, in alcoholism, in multiple sclerosis, in apoplexy, and in other diseases which were not distinctly luetic in origin. Nonne was the first to treat this question exhaustively, with the following results: There was a marked lymphocytosis in 97 per cent. of cases of dementia paralytica; in 96 per cent. of tabes; in 76 per cent. of tertiary lues of the central nervous system; in 50 per cent. of secondary syphilis; in 100 per cent. of congenital lues; and in 32 per cent. of those who had passed through specific infection without showing any symptoms at the time of examination. On the other hand, it was found in only 35 per cent. of chronic alcoholism, in 15 per cent. of epilepsy, in 40 per cent. of apoplexies, in 23 per cent. of multiple sclerosis, in 40 per cent. of tumor cerebri; whereas in neurasthenia and hysteria none showed a lymphocytosis, and there was positively no lymphocytosis in any form of psychosis without preceding syphilis, nor was it found in any patients who, whatever other disease they may have had, exhibited no symptoms of disease of the central nervous system. A markedly positive lymphocytosis was found only in tabes, general paresis, cerebrospinal syphilis, congenital lues and acute meningitis. We thus find corroboration for Schoenborn's statement that the increase of cellular elements is an almost constant and early symptom of tabes and general paresis. It represents one of the earliest diagnostic signs, and one should not fail to make this test in any cases in which there is a suspicion of tabes or general paresis.

Erb stated later on that in cases in which a positive lymphocytosis is found the diagnosis of tabes is rendered absolutely certain, and this is true for general paresis also. In my own experience the truth of these statements has been fully borne out. In private practice, where patients so frequently present themselves for cursory examination, the test cannot be so easily made. Altogether it is well to caution practitioners against any attempt to decide a doubtful case by hasty withdrawal of the cerebrospinal fluid, or by hasty examination of such fluid. Lumbar puncture is not a procedure to be undertaken lightly, although I have never personally had any difficulty and have been fortunate enough not to be responsible for a single case of infection. At least one case—and a very sad one—has come to my notice, which I have been privileged to see in consultation, in which no other conclusion could be reached than that a general septicæmia had followed upon a lumbar puncture done for diagnostic purposes in a case in which syphilis of the central nervous system was suspected. And speaking of cases in which lumbar puncture should not be done, I consider it my duty to call special attention to the fact that one should hesitate to do lumbar puncture in cases of cerebellar disease, and in cases in which there is reason to suspect serious trouble in the posterior fossa. The withdrawal of lumbar fluid is apt to bring about a difference in pressure of so marked a character that a neoplasm near the fourth ventricle may, with great suddenness, produce pressure upon the respiratory and cardiac centres in the medulla, and thus bring about a fatal termination. I have had to do lumbar puncture a few times, both in children and in adults, in which disease of the posterior fossa was suspected. In these cases the fluid was withdrawn without untoward result, but I observed the precaution of withdrawing the fluid slowly, drop by drop, of withdrawing very little, only 2 or 3 c.c., and of placing the patient during the lumbar puncture and for hours afterward with the head dependent and the feet elevated. Lumbar puncture should only be done if the patient can be kept in bed for at least 24 hours after the puncture has been made.

If these precautions are observed the procedure becomes an extremely valuable one. In tabes and general paresis the lymphocytosis is almost pathognomonic, and it helps us in hospital practice to

distinguish easily between syphilis of the central nervous system and other forms of disease, disseminated sclerosis for instance. Let me refer briefly to two cases which are at the present time in my wards at Mount Sinai Hospital:

The one was the case of a young man 23 years of age, who presented peculiarities of speech, which was drawling rather than scanning, a slight nystagmus, a very marked spastic paraplegia, and a slight intention tremor. His gait was spastic, and this spasticity was functionally exaggerated. The pupils were normal. There was at a very early period of the disease a more or less apathetic mental condition, so that while the symptoms pointed to a disseminated sclerosis, there was also the possibility of a diffuse cerebrospinal syphilis. Lumbar puncture was done in this case and the fluid that was withdrawn showed no increase of cellular elements; one or two in every 3 or 4 fields, small and large lymphocytes were equally distributed. On the strength of this no attempt at antiluetic treatment was made, and the diagnosis was decided in favor of disseminated sclerosis as against syphilis. About a week later Wassermann and Noguchi tests which were made were also negative, so that there was double reason to abandon every suspicion of lues. The further development of the case has fully substantiated these findings. The speech is now distinctly scanning, the intention tremor has become most marked, there is a typical tremor of the head and the clinical picture is altogether that of a disseminated sclerosis.

The other case is that of a woman of about 40, who during the last few years had developed a slowly increasing spastic paraplegia without any history of trauma, without any antecedent myelitis, with all the attendant symptoms of exaggeration of the reflexes, and contractures; the pupils were mobile, there was no history of headaches, so that we were much in doubt as to whether this spastic paraplegia was due to a disseminated sclerosis, as it often is, or whether it was the expression of a spinal syphilis. In this case the examination of the lumbar fluid revealed a most intense lymphocytosis. The increase of cellular elements was so great that there could be no doubt whatever of the syphilitic origin of the trouble. At least, there was no doubt that the patient had had an antecedent syphilis. On the strength of this examination she

was for the first time subjected to marked antisymphilitic treatment by hypodermatic injections of sublimate—a method which I employ to the exclusion of all others—and after six injections a very marked improvement had set in and the patient, who was almost bedridden, is now able to get about very satisfactorily and a few days ago was able to return to her home.

I could instance other cases of the sort. We might refer to another patient, a man of 35, a laborer, who had had some slight nystagmus, transitory ocular palsies, very slight spasticity, and a transitory interference with vesical and rectal symptoms; no disturbance of speech, however, and no marked intention tremor. Here again the question arose as to whether the case was a disseminated sclerosis or a cerebrospinal syphilis. The examination of the lumbar fluid gave evidence in favor of syphilis, and I refer to this case more particularly because the withdrawal of the fluid acted so favorably upon the patient that he himself requested repeated punctures, and during a period of eight weeks, while he was kept under observation, three lumbar punctures were made. The result of the examination was the same in every instance, and after each puncture the improvement was very marked. This improvement after lumbar puncture I have observed a number of times and I can well conceive that, particularly in syphilitic affections of the central nervous system, with the numerous adhesions between the pia, the dura, and the brain or spinal cord substance, there is apt to be a stasis of cerebrospinal fluid which may be relieved by puncture.

Schumm and Apelt, working in Nonne's clinic at Eppendorf, reported upon the albumin content of the cerebrospinal fluid. The method is as follows: 85 Gm. of the purest sulphate of ammonium (Merck) are put with 100 Gm. of distilled water in an Erlenmeyer flask, and boiled for a period of time until no more of the salt is dissolved. The mixture is allowed to cool and is filtered. The filtrate represents a saturated solution of ammonium sulphate, and has the power of precipitating globulins and nucleo-albumins. Equal parts of the liquor cerebrospinalis and of the reagent are mixed and allowed to stand for three minutes in the cold. After three minutes the result is noted, and according to the intensity we may have either cloudiness, opalescence, weak opales-

cence, or only a trace of opalescence, the latter being practically negative. To this procedure Nonne has given the term "Phase I." According to his statistics this "Phase I" was positive in all of 59 cases of dementia paralytica; in 69 per cent. of the cases of tabes, and in 69 per cent. of tertiary syphilis. On the other hand, whether the patient had had preceding syphilis or not, it was invariably absent in other forms of central nervous disease. Inasmuch as it is universally present in dementia paralytica, and almost as frequent in tabes, even in the earliest stages, and is never present in other diseases of the central nervous system whether the subject be syphilitic or not, Nonne is correct in asserting that it is a far more delicate test in the case of tabes and general paresis than is the ordinary cyto-diagnosis. Moreover, he attaches the greatest possible importance to the fact that this "Phase I" was entirely negative in cases in which the syphilitic infection had been cured, whereas in cases of tertiary lues of the central nervous system it was present in all of 29 cases—so much for these two methods.

For some reason the preceding methods have not obtained the general recognition accorded to the Wassermann reaction. Inasmuch as I have reported upon the "Wassermann Reaction in its Relation to Diseases of the Central Nervous System" only a few months ago before the Neurological Section of the American Medical Association, I may review briefly a few of the points which I recorded in that paper, and may refer to some additional experience.

I will say nothing of the relative value of various modifications which have been proposed, as my experience has been chiefly limited to the original Wassermann method, and I may be permitted to express the hope that in spite of the ingenuity and the excellence of the modifications which have been proposed, the original method should not be slighted. Wassermann's method has been found satisfactory in thousands upon thousands of cases. There can no longer be any doubt as to its general value, and it is already a greater help in clinical diagnosis than any similar procedure which has come to us from the laboratories. My experience is based on observations made upon more than 300 patients at Bellevue, New York State, and in private practice, upon many of whom repeated tests were made. A positive Wassermann reaction, I am firmly

convinced, means active syphilis. A negative reaction, unfortunately, does not exclude syphilis, but if the reaction is carefully done a positive finding is of such incalculable value that we must not mourn for the failures in case the reaction turns out negative. As with the Widal reaction, a negative reaction may not altogether exclude typhoid, but at least it renders it improbable, and so it is in a very large proportion of the cases of syphilis of the central nervous system. As I said in a previous communication, in a vast majority of cases in which the negative reaction is obtained the thought of syphilis may be dismissed. In a large number of others in which a positive reaction has been found present at the beginning of the disease, and in which a negative reaction has been obtained during or after prolonged treatment, it is only fair to assume that the syphilitic virus has been neutralized as the result of the therapeutic measures employed. Hoehne, writing in the *Berliner klinische Wochenschrift* of May 10, 1909, has shown conclusively that the Wassermann reaction is influenced by mercurial treatment and by definite forms of mercury, sublimate holding a very high rank. Wassermann and his school laid special stress upon the value of the reaction in tabes and general paresis. It was my feeling very soon after the publication of the first reports, that we neurologists did not need evidence of specific disease nearly as often in tabes and general paresis as we did in other affections of the central nervous system. The reaction, however, gave very important corroboration of the syphilitic origin of these two diseases. The first investigators reported the percentage of positive reactions as high as 95 per cent. in general paresis and 90 per cent. in tabes. In my own series of 28 cases of tabes only 64.3 per cent. were positive, and in 31 cases of general paresis 67.7 per cent. were positive. These figures are very much lower than those of the German investigators, and allowing for every difference in the interpretation of results and possibly in the method, although the methods adopted by myself were those of the Wassermann school, I believe that the lower percentages obtained in my series are largely to be attributed to the practice of subjecting every case of tabes and general paresis to mercurial treatment. Allowing for the frequency of positive reactions in tabes and general

paresis, as well as in other diseases of the central nervous system, the question arises whether a positive reaction may be taken to be pathognomonic of the disease, or whether it simply proves that the blood of such person contains active syphilitic virus. After a prolonged experience, I cannot consider a positive reaction as establishing anything more than an antecedent specific infection, since we find it in other diseases of the central nervous system that are clearly due to syphilis. Alt, writing in a recent number of the *Münchener medizinische Wochenschrift*, inclines to somewhat the same view and concludes that in most cases of general paresis there is not only an active syphilitic virus in the blood, but that the general parietic is also a carrier of spirochætæ.

It would be repeating the experiences which I detailed in my former publication, if I were to recite cases proving the value of the Wassermann reaction. I will only repeat what I have said before, that the reaction has been of greater service to me in other syphilitic diseases of the central nervous system than in tabes and general paresis. In the question of the differential diagnosis between disseminated sclerosis and multiple cerebrospinal syphilis, a positive Wassermann reaction has been found to be of the greatest benefit. In disseminated sclerosis it is invariably negative. A patient of mine whom I have had under treatment for years, first with hemiplegia then with spastic paraplegia due to preceding syphilis, and who during the past year had exhibited loss of vision of one eye and the signs of a distinct specific retinitis, has not only been found to have a positive Wassermann reaction, but during a period of fifteen months I have been able in his case to establish the fact that the reaction varied according to the intensity of the symptoms. At three different periods, with a lessening of the reaction, vision has improved, and when the vision grew worse the blood was again found more positive. In this case, as in others in which there has been a possibility of recurrence of syphilitic disease, I have established the rule, both in hospital and private practice, that the patient should return for the examination of the blood every few months, and that the propriety of giving mercurial treatment should be determined by the character of the reaction. A patient whose blood, after having been found positive at the beginning of treatment, has become negative during or immediately

after a course of mercurial injections, should be resubjected to mercurial treatment if the reaction again becomes positive.

If we allow for the assistance given us in cases of tumor of the brain—and nowadays no such cases should be operated upon unless the Wassermann test has been made—if we allow for the light thrown upon doubtful cases of hemiplegia, and, above all, for the information gained in cases of mysterious epilepsy beginning late in life, we can appreciate the enormous value of this test. Whatever the difficulties may be in the way of interpreting the Wassermann reaction, whether it be self-contradictory or not, whether it contains some slight pitfall or not, we feel that there has been no new clinical method of the last two decades that can at all compare in value as an aid to diagnosis with the Wassermann test—and may I here also add that it will prove to be of greater value as time goes on in determining our therapeutic procedures. The direction in which the wind is blowing is shown by a recent contribution of Alt, who has advised the use of arsenophenylglycin in general paresis. He bases this recommendation upon researches which were evidently conducted along the lines personally laid down by Ehrlich who, after finding atoxyl unsatisfactory and dangerous, has been casting about for other substances which would be likely to influence the luetic virus. As a matter of fact, it has been found that the Wassermann reaction disappeared promptly after injections of arsenophenylglycin. It is supposed to have an influence on lecithin metabolism and in this way possibly to affect the syphilitic poison. Whatever the explanation of this may be, it already points to at least one therapeutic measure suggested by the Wassermann test, which may be of service in the incipient stages of general paresis. As far as disease of the central nervous system is concerned, the presence of a positive Wassermann reaction is an indication for antisymphilitic treatment, and in this order of diseases, to my mind, it calls for treatment by mercury, and preferably by mercurial injections.¹ While specific headaches and milder

¹ During the past six years or more I have depended altogether upon sublimate tablets recommended by the late Dr. S. S. Jones. Each tablet contains sublimate (gr. $\frac{1}{4}$), cocaine hydrochloride (gr. $\frac{1}{16}$), sodium chloride (gr. $\frac{1}{4}$). Boil the tablet in a test-tube with 60 c.c. of water; pour into a watch glass or a sterile dish and draw up into an all-glass hypodermic syringe; then make a deep intramuscular injection in the gluteal region—change needles frequently. If given in this way, the injections are painless, and most satisfactory.

specific conditions may yield to the administration of iodides, specific myelitis or any serious specific invasion of the cord or brain is benefited only by systematic mercurial treatment. The recent interesting statistics of Hoehne showed that calomel and sublimate injections are the most efficient. According to this writer the Wassermann reaction is changed from positive to negative more often after the administration of these two mercurial preparations than after other forms of treatment.

The Wassermann reaction, then, is a great addition to our diagnostic methods; as a guide to our therapeutic efforts it should be practised regularly in every neurological ward, and a knowledge of it must be part of the equipment of every neurologist.

Diagnosis and Treatment

SYMPTOMATOLOGY OF PELLAGRA

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DEFINITION

PELLAGRA is an endemic disease attributed to eating Indian corn infected with certain *Hyphomycetes*. It is characterized by digestive disorders, symmetrical dermatitis on parts of the body exposed to the sun or subjected to constant pressure, various mental phenomena, principally depression, and in most cases by symptoms referable to spinal degeneration.

SYMPTOMS

The malady is so insidious in its onset that it is difficult to state absolutely what are the earliest premonitory symptoms. The first thing usually complained of by the patients is some gastrointestinal disorder; this may be loss of appetite, burning sensation in epigastrium, excessive desire for food or drink, or more often diarrhœa with more or less stomatitis and salivation. Soon after these digestive disorders manifest themselves, or coincidentally with them, the patient detects a disinclination to any exertion, becomes irritable and sleepless. Duties that were formerly dispatched with a feeling of pleasure are now looked upon with a dread; and procrastination takes the place of habits of promptness; so that the personal appearance of the victim, or the aspect of the home and children, if the sufferer is a woman, indicates neglect; all of which is evidence of the psychic depression that forms later a prominent figure in the clinical picture of the disease. After these symptoms have persisted with usually increasing severity, in some cases for weeks, in others for months, the characteristic

symptom of the disease almost invariably appears, namely, erythema on the dorsum of the hands and arms not covered by the clothing.

THE SKIN ERUPTION.—This may be either *dry* or *wet*.

Dry Form.—This eruption appears usually in the early spring months, and while it is the most characteristic objective feature of the disease, it is subjectively one of the least important, as very few of the patients suffer any physical discomfort from it other than a burning sensation, complaining principally of the unsightliness. The eruption commences as an erythema suggesting sunburn on the backs and hands, and extensor surface of forearms, extending up the arms to the point that the sleeves reach, and ends abruptly there, being absolutely symmetrical if the sleeves are symmetrical, which is usually the case. There is cedema at the site of the erythema, in proportion to the severity. In persons who do not “hold their hands” the eruption extends to the flexor surface in a characteristic shape—commencing on the radial border it extends toward the ulnar by an oblique line forming a patch of erythema on the flexor surface somewhat triangular in shape, the base of the triangle being the radius and the apex near the styloid process of the ulna. Patients who are well advanced in the disease and unable to work, and who “sit about” and “hold their hands” have the eruption on the flexor surface to the same extent as on the extensor surface. The erythema lasts for a few days and then commences to fade, and the skin begins to desquamate in fine scales if the dermatitis has been mild. As the redness fades the site of the erythema assumes a somewhat cyanotic hue, this is gradually replaced by a characteristic light-liver or chocolate color, which once seen cannot be mistaken or confounded with any other skin disease. In negroes it is readily recognized by an increase of pigmentation, the site of the eruption appearing as though soot had been smeared on that part of the hand and arm.

The patients often make vain attempts to remove the dirty appearance of the hands with soap and water. After a time this eruption scales off and leaves the hands soft, velvety and glistening—quite a contrast to the dirty hands that they were the sorrowful possessors of only a few weeks before—but like Banquo’s ghost, it has come to stay for a term—the erythema reappears, and the eruption follows the same course as previously described;

this may happen several times during the summer. As a result of these repeated inflammations the skin of the hands become thickened, hard, wrinkled and inelastic, and frequently deep fissures form, which are quite painful, so much so that the fingers cannot be flexed, the index finger at or near the first joint being especially liable to become cracked. Portions of the body covered by the clothing subjected to pressure also show the eruption in some cases, the skin over the olecranon, trochanter, sacrum and knees being especially liable to become affected. The mucocutaneous junctions are also affected, especially around the anus and vulva. The forehead, face, and neck, are often the seats of the eruption. In those who go barefooted the feet and legs do not escape. The palms of the hands usually escape, but not always. The eruption commences in the spring months and persists until July, August, or September, and then disappears to make its appearance in the following spring. In some cases there is a mild relapse in October. The crowning characteristic of the pellagra eruption is its symmetry and color.

After the discolored skin has been exfoliated there usually remains a fringe of dirty epithelium, a relic of the line of demarcation of the dermatitis. In some cases the sebaceous glands on and around the nose are hyperactive and enlarged, there being a seborrhœa. Purpuric spots are sometimes seen in the hands and face, a favorite site being under the eyes, here the spots have a crescentic shape, and are symmetrical. In some cases the upper lid is also involved, the appearance of the eye resembling that due to trauma in this locality, except that the conjunctivæ are not affected. On the hands these spots are sometimes on the palmar surface, and are very prone to become bullæ, containing serosanguineous fluid.

Wet Form.—This differs only in degree. Where the dermatitis is severe, bullæ form, sometimes containing serous, serosanguineous, or seropurulent fluid; when the bullæ break large ulcers are left to mark their site, or large flakes of skin desquamate, leaving a raw surface; slight cicatrices remain as an evidence of former ulceration, "the whole clinical picture being analogous to a burn of the first degree" (Dr. Babcock).

The wet form involves a greater area than the dry, such as

axillæ, groins, etc. This form has been frequently diagnosed as dermatitis exfoliativa. The eruption is an index of the severity of the disease; an extensive, severe eruption usually bespeaks a severe infection.

DIGESTIVE DISORDERS.—The buccal mucosa becomes very red, the tongue and mucosa of lips showing particularly this characteristic symptom. If the throat is examined this redness will be observed as far as one can see into the pharynx. Flakes of exfoliated epithelium will be seen adhering to the gums, and the tongue, being denuded of its epithelium, is smooth and glistening. Its color being a cardinal red and it being a cardinal symptom of the disease, I have denominated it the cardinal tongue. Sandwich calls it the "bald tongue." This stomatitis is accompanied by a very profuse flow of thick saliva, in some cases so profuse that the saliva dribbles out of the corners of the patient's mouth. Ulcers often form on and under the tongue and are quite painful. Intelligent patients suspect that they have been salivated by mercury. When the mouth is open strings of saliva will extend from the upper to the lower teeth. My attention was directed by Dr. Babcock over a year ago to small black or bluish-black spots on the tongue, and since then I have observed these papillæ in a number of cases, all negroes. The name of "stipple tongue" has been given this condition by Dr. Lavinder. The tongue may be either pointed and tremulous, or large, flabby, swollen, and indented.

The salivary glands may be swollen and tender, this with the salivation and condition of the swollen gums has been mistaken for mercurial salivation, but remember that in mercurial salivation there is always quite a disagreeable odor to the breath, and while there is an odor to the salivation in pellagra, it is not the same disgusting fetid odor that is characteristic of mercurial ptyalization.

The acme of the stomatitis corresponds in point of time and severity to the acme of the eruption on the hands. Other mucous membranes are also inflamed, proctoscopic examination revealing a bright red mucosa as far up the gut as can be seen.

Hemorrhoids are sometimes complained of. One of my patients thus complaining showed on examination only an intense redness of the mucosa, still she insisted that she suffered acutely

from piles. This patient was then in a state of mild delirium, and probably there was some irritation that caused her to refer to trouble in that locality. She was far advanced in the disease, and this was the only symptom complained of. It is not unusual, however, for patients to complain of discomfort in this locality, especially is this so when there is a skin lesion around the anus. The mucosa of the vagina is also a seat of inflammation and vulvovaginitis is not at all infrequent.

Stomach.—A burning sensation in the œsophagus, or stomach is quite frequently present. Pyrosis is sometimes a prominent feature with or without belching. "Pyrosis is never absent" (Lombroso). Vomiting occasionally occurs, but is not a constant feature of the disease. When the disease is advanced dysphagia is complained of by some patients, and this may be accompanied by strangling when fluids are taken.

Marked gastric symptoms are in evidence in some cases. I have known a case of pellagra diagnosed as gastric cancer. The only abnormality detected by abdominal section was an excessive redness of the peritoneal coat of stomach. After a few days the patient was rolled out into the sun and soon there appeared on her forehead and hands an intense erythema. This aroused suspicion, and two competent consultants were called in. From the history of repeated attacks of eruption, and the picture presented by patient, the diagnosis of pellagra was made, and the subsequent course of eruption (color, etc.), tongue, diarrhœa, and depression, put the diagnosis beyond doubt.

Diarrhœa.—This is a feature of the disease at some time in its course. It varies from a few soft stools a day to twenty or more; sometimes they contain blood and mucus; they are frequently involuntary even when the patient's mental attitude is good. In a number of cases I have noticed that the stools were as frequent at night as in the day. The diarrhœa is obstinate and not affected by the ordinary treatment or diet. I have seen it persist in spite of large doses of bismuth and opium and a rigid diet, and improve when drugs were discontinued and diet not restricted. It is not dependent upon errors in diet, but is a neuropathic manifestation, due to disease of the spinal cord and the sympathetic system.

The fact that the normal reflex in the intestines is greatly increased by the pathological changes in these structures, may explain the diarrhœa; since it produces hyperperistalsis, in the same manner as irritants applied to the skin produce an exaggerated vasomotor dilatation with erythema as a result.

In rare cases there may be constipation. These cases are very mild and show very slight mental depression or none at all. In the terminal stage when a rising temperature sets in the diarrhœa sometimes stops. Hemorrhages from the bowels may occur. Meteorism is present with the diarrhœa and sometimes persists after the bowels have lost their frequent action. The diarrhœa follows the same course as the erythema and stomatitis, the acme of severity of the diarrhœa being synchronous with the acme of erythema and stomatitis; it has exacerbations and remissions and persists through the spring and summer months, with a slight recrudescence in October, usually disappears during winter, and reappears the following spring. Occasionally it is only remittent, having exacerbations and remissions the whole year.

PUPILS.—Pupillary abnormalities are quite striking in some localities and in some seasons, varying in the same locality from year to year. In the year 1908 in South Carolina, pupillary dilatation was the rule, the mydriasis being extreme in some cases. It may be either bilateral or unilateral; if unilateral the right pupil is most apt to be dilated. During this year, 1909, I have seen few cases with dilated pupils, contraction of pupils is sometimes met with. The pupils react sluggishly to both light and accommodation and “resist the action of homatropine considerably longer than the normal” (Dr. Whaley). Diplopia and photophobia are not unusual. These pupillary phenomena must be due to a disturbance in the ciliospinal centre. This centre is situated in the spinal cord between the first cervical and second dorsal nerves—the portion of the cord that is nearly always affected in pellagra.

PAIN IN THE BACK.—This was a striking feature in some of the Italian cases that I saw, the pain being so severe that the sufferers walked stooped over, this attitude furnishing one of the seven varieties of the disease described in the Italian proverb. I have had only a few patients complain of pain in back among the

number studied in America. Pains in various portions of the body are often complained of. Tenderness at some point along the spinal column is almost constant. It is usually in the mid-dorsal region and is easily elicited by pressure with the fingers along the spine. The tenderness varies on the two sides, in some cases being more acute on the right. The tenderness is not over the spinous processes, but over the point where the nerves emerge from the canal.

TEMPERATURE AND PULSE.—The mild cases are practically afebrile, *i.e.*, temperature less than 100°. The morning temperature is often sub-normal—96° to 97.5° F. Temperatures of 102° to 108° or over are not unusual in cases progressing to a fatal termination from so-called typhoid pellagra, as the accompanying charts will show (see page 49, Figs. 1, 2, 3, and 4).

The pulse is accelerated to 80 or 100 in ordinary cases, but increases with the toxæmia or temperature, and counts of 160 are not unusual in fatal cases. Very rapid respiration is occasionally encountered without any appreciable cause for it.

There is nothing characteristic about the urine, except the amount is diminished to 500 to 800 c.c. (18 to 25 ozs.) in 24 hours and that "alkaline urine is a bad prognostic sign" (Lombroso).

The reflexes are usually exaggerated, though they may be normal, diminished or lost. Like other signs, they vary with locality and season. The patella reflex is especially lively, the slightest touch eliciting a lively jerk; the knee-jerk varies on the two sides, in some cases, being more lively on the right, the side that has the most exquisite spinal tenderness. In very severe cases, or rather those in which there are tetanic contractions, ankle clonus may be found. The Babinski reflex is sometimes obtained. In those cases that are paretic the reflexes are abolished. There is usually analgesia or anæsthesia at the site of the eruption.

Vertigo is complained of by nearly all of the sufferers, and should always be asked about, if not mentioned by them. Its presence should always excite suspicion, and other pellagrous stigmata sought for.

PSYCHIC PHENOMENA.—Briefly, mental depression is as constant as the erythema and diarrhœa, and varies from a mild case of the "blues" to severe melancholia. The patients seem to have

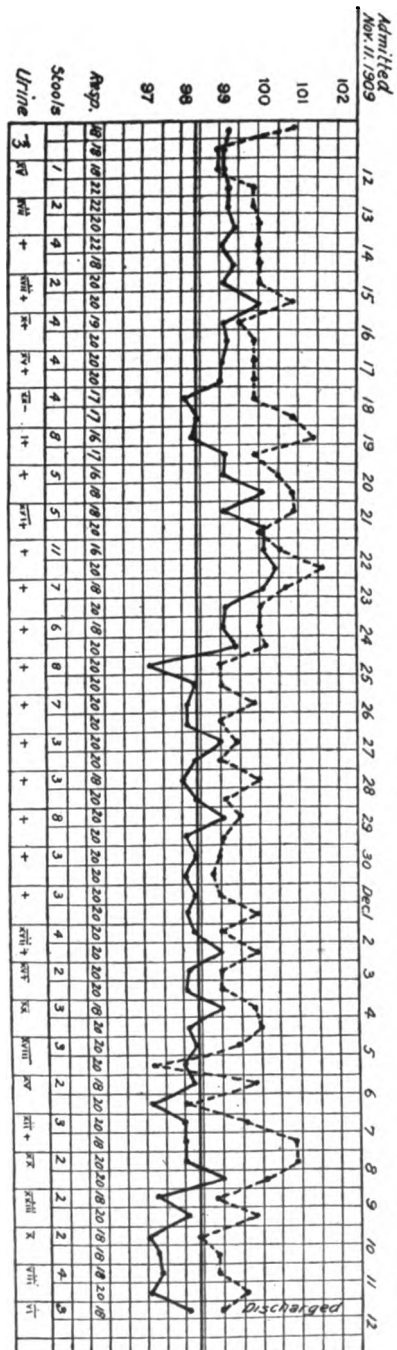


Fig. 1.

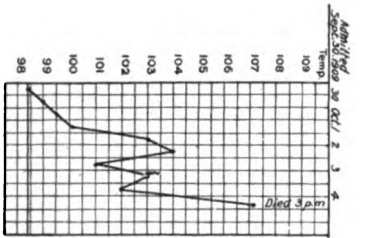


Fig. 2.

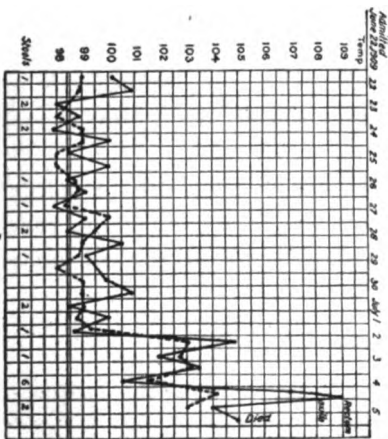


Fig. 3.

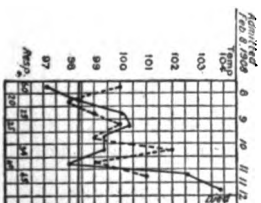


Fig. 4.

Typical temperature charts in pellagra, the three smaller charts illustrating "typhoid pellagra," with death.

"forgotten how to laugh." The poor sufferers imagine they have not a friend on earth, that even their own children and parents dislike them, and have some irreconcilable grievance against them. They are easily provoked to anger, and in many ways indicate lack of mental force. Hallucinations and delusions are sure to occur at some time in the disease, and no two patients will have the same delusions. In Italy 10 per cent. become insane. As yet we cannot form any opinion as to what portions of our patients will become insane, but if statistics are properly kept it will be a very easy matter to ascertain what proportion is demented. In some cases the facial expression is characteristic, the brow being contracted and wrinkled, and suggesting profound introspection and mental depression.

While pellagrins are never loquacious, at times they complain of real or imaginary ills. As the disease advances they talk less, often not answering questions, and finally pass into a state of absolute *mutism*. This portion of the pellagrous syndrome is very important, and pellagrous insanity properly calls for separate consideration.

GAIT.—The gait is either spastic, simple paralytic, or paralytic spastic. The patients walk with their legs far apart, and as paresis sets in the stride is very much decreased and the patient assumes a peculiar shuffling gait.

PROGNOSIS

Of course, as in all other chronic poisonings, the earlier the condition is recognized and conditions remedied the better the prognosis. Mild cases even of several years duration show marked improvement, if not complete recovery, when put upon a proper dietetic and hygienic regime.

The surroundings of the sufferer influence the prognosis. If he is financially able to carry out instructions, obviously the prognosis is better than if the reverse is the case. Cases of severe infection, manifested by extensive dermatitis, severe depression and diarrhoea, require a guarded prognosis. Temperature above 102° F., independent of an intercurrent disease, is a serious symptom, and more so if there are evidences of neuromuscular irritability.

The so-called typhoid pellagra is universally fatal. Hemor-

rhages from either stomach or bowels are an evil omen. The susceptibility to tuberculous infection, as a result of the lowered resistance incident to the disease, should be kept constantly in mind, especially in institutions. The outlook is more gloomy in women than in men. Patients seemingly progressing toward a favorable termination may die suddenly, from cardiac paralysis, or more slowly from hypostatic congestion of lungs.

Pellagrous insanity has a mortality of 50 per cent. to 70 per cent. in the United States. "When the disease has recurred for 3 or 4 seasons and especially if the mind is affected the prognosis is very bad. I gathered from the physicians of Italian lunatic asylums that recovery of patients once arrived at the asylum stage of insanity is almost unknown. Still these are extreme cases; the mentally afflicted in their earlier phases may recover. Only too often, however, the advance to death is inexorable" (T. C. Allbutt, "Allbutt's System of Medicine," vol. ii, 1907). Our experience in South Carolina, I am sorry to say coincides with Allbutt's observation.

CASES

CASE I.—Mrs. T., white, widow, no children, age 62, family history good. Always in good health until present illness, which commenced December 1, 1907 with diarrhœa and lack of energy. The diarrhœa gradually became more severe and the motions were as frequent at night as they were during the day. About January 1, 1908, mouth was quite sore and salivation extreme, mental depression and weakness gradually increased until she was forced to take to her bed about May 1. The eruption appeared on hands about March 15, and was so severe that her physician thought she had gangrene, temperature ran for three weeks from 100° to 101° F. May 23, admitted to Columbia Hospital, weight 89 pounds. Visceral examination negative. Urine normal, pulse 68, temperature 96.5° F. There existed on hands and forearms patches of pellagrous eruption, the dirty fringe being very noticeable. The palms of the hands were exfoliating and had been the seat of an intense dermatitis, bullæ having formed on them containing seropus. She endeavored to keep her hands concealed, as they were unsightly, and did not care for any one to touch them, fearing

that she might contaminate them. There was also a patch of dermatitis on each elbow about the size of a half-dollar. Tongue and buccal mucosa very red, saliva profuse and tenacious. Patellar reflexes exaggerated, right most lively, pupils contracted, tenderness in mid-dorsal region, right side more tender than left, vertigo on standing. She remained in hospital until November 30, 1908. During that time she had frequent remissions and exacerbations of diarrhoea, they being most severe from time of admission until about August 1, when her physical condition gradually commenced to improve. The greatest number of stools was in July (16th) when fourteen were recorded in twenty-four hours. The stools were principally involuntary from May 30 to August 3. Bed-sores appeared June 12. Nausea and vomiting, June 4, and continued until July 15. All medicine including bismuth and opium was discontinued July 13, and July 15 there was no nausea or vomiting. Herpes zoster developed September 16. As her physical condition improved her mental condition became worse, she imagined she was covered with microbes and every day would have great number of fibres of lint and wool in a pus basin to show me the "things that were tormenting her to death." The latter part of November she became excited and it was thought best to transfer her where she could be restrained. She was sent to a private institution in the North and remained there until June of this year. There has been no recurrence of the diarrhoea or eruption, she is the picture of perfect health to-day—weighs 130 pounds.

She admits being very fond of corn-bread, that she ate it every day. She also states that for months before she was taken sick that neither her corn-bread nor hominy were properly cooked, the servant she had at the time being very careless.

CASE II.—Mrs. S., age 21, white, married, three children living, four dead; no miscarriages, native of North Carolina. Husband country merchant, distributing considerable quantities of shipped goods, including corn by carloads. Health always good until four years ago, when she presented the pellagrous syndrome, diarrhoea, eruption on hands, stomatitis, salivation, and vertigo. These lasted all spring and summer, disappearing during winter; they have returned each spring with increased severity. The first

year the symptoms were noticed quite a number of young chickens in the yard lost their feathers, were very red, did not grow, and finally became ataxic and died. She was in a state of valetudinarianism practically for four years; being frequently accused by her husband of being hysterical, as she often cried, was apprehensive that something dreadful would happen her. In February, 1909, complained of burning in stomach; later diarrhœa, eruption and salivation appeared, the symptoms being more severe than at any previous attack.

Condition June 13, 1909: fairly well-nourished woman, facial expression that of melancholy, absolutely mute, patellar reflexes absent. Pupils dilated, cardinal tongue, strings of saliva extend

Fig. 5.

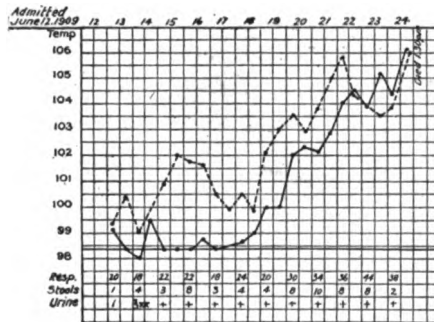


Chart of Case II.

from upper to lower teeth when mouth is open. Takes no interest in surroundings or conversation, thus being without insight. Remnants of pellagrous eruption on hands and elbows. Has always eaten bought meal.

Hospital Record.—Upon admission was restless, deluded, probably subject to hallucinations, required constant watching. Full tub baths had a soothing effect for a time, the baths following the nervous manifestations.

June 14, was nervous, restless, noisy and deluded.

June 15, same condition except stools frequent and involuntary.

June 16, involuntary stools, but quiet.

June 17, refused food, quiet.

June 18, rested quietly, bed-sore.

June 19, fairly quiet, temperature and pulse both elevated and

limbs slightly rigid and tremulous, low muttering delirium, continuous rectal irrigation was commenced. The temperature gradually rose and the neuromuscular manifestations became more accentuated until the condition reminded one of strychnine poisoning. Evidences of intense toxæmia present,—low muttering delirium, carphology, subsultus and dry tongue. All of these symptoms continued with increasing severity until the morning of June 24, when death closed the scene (see Clinical Chart Case II, Fig. 5).

CASE III.—Before taking up the anamnesis of this case it will be necessary to review the family history; although the patients were not seen by me.

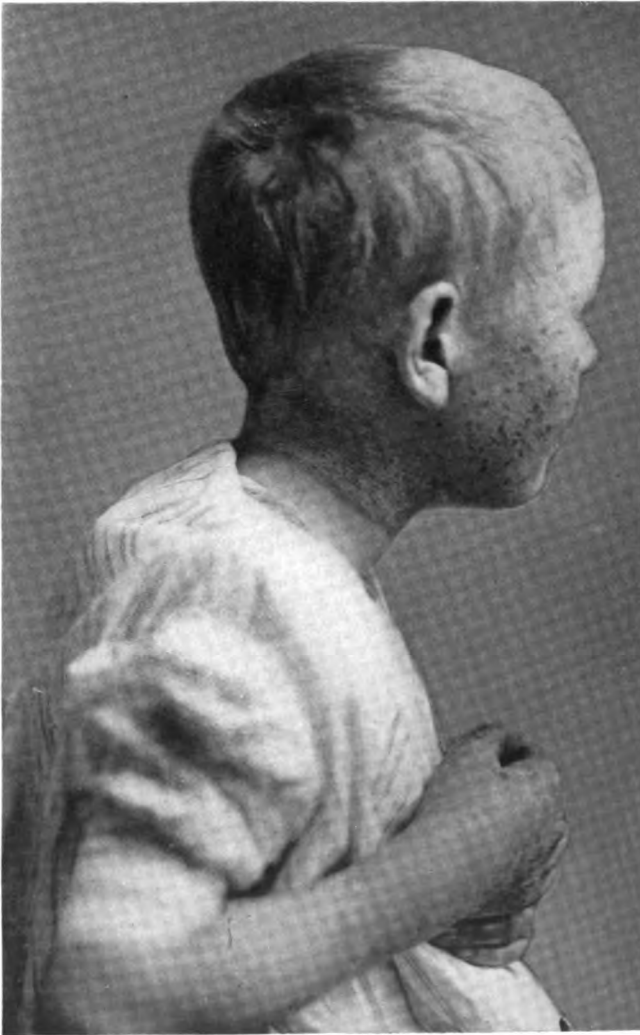
L. C., male, age 11, parents living, father being a miller. One sister died three years ago of pellagra at 14 years, and brother of same disease at 11 years, four years ago. Both died in August, the two cases having developed the disease in their fifth and fourth years respectively. The disease manifested itself in the spring, and was supposed to be ivy poisoning. Remissions and exacerbations occurred during the spring and summer, and in winter the dermatitis and diarrhœa were entirely absent. The disease increased in severity for six years in the case of the boy until finally after being unable to walk for two months, he was confined to bed four months, and, following one month of excessive vomiting and diarrhœa, died of exhaustion. On several occasions he vomited dark clotted blood. The girl had the disease mildly at first, sore mouth, diarrhœa, and eruptions on hands and feet. With her the disease lasted nine years. She had vertigo, burning in stomach, pain in back of neck and between shoulders, head drawn back, high fever; was treated for "spinal trouble" and "hysteria." There was a tendency to stagger and fall backwards after any exertion. This was a striking feature of the case for the last two years of her life. There was no vomiting till shortly before death, nor was the diarrhœa so severe as in her brother's case. In April 1906 she complained of intense burning in stomach "like she was burning up." The eruption, stomatitis and diarrhœa then appeared, and she soon became very weak and was confined to bed till August, when she died, evidently of typhoid pellagra. For about two weeks before death she had convulsions with increasing frequency. There were hemorrhages from bowels; opisthotonos,

FIG. 6.



L. C., Case III, showing lesions of pellagra on face, arms, and hands.

FIG. 7.



L. C., Case III, showing "pellagra mark," the sharp ending of the eruption on the portion of the neck covered by the skin; this line of demarcation is the same on the other side of the neck.

FIG. 8.



Pellagra eruption, showing its symmetrical arrangement : desquamation has already commenced on the right hand.

FIG. 9.



Negro boy—pellagra for 5 years; died of tuberculosis 10 days after photograph was taken.

arms and legs rigid, mouth quite tremulous "like she was chewing"; subsultus marked; and for the last week of life, temperature was very high.

These histories are obtained from the father and mother. Furthermore the father states that these children, as soon as they were old enough to accompany him to his work, when playing about the mill-house frequently ate raw meal hot from the rock. The first year that either of the children was affected, he remembers that the local corn crop was practically a failure the previous year, and that he ground a great deal of shipped corn that he knew was damaged, spoiled or rotten.

So far as can be learned neither the father nor the mother has at any time had the symptoms of a disease that suggests pellagra. It should also be recorded that the disease was not recognized as pellagra during the lives of these two children. Furthermore, the father states that so far as possible he selected the best corn only for his family use. This may explain why the parents escaped, while the children who ate the raw meal of any sort contracted pellagra.

Personal History.—Affected for nine years, the pellagrous syndrome, dermatitis, stomatitis, and diarrhœa appearing every year in the spring. The diarrhœa has never been severe—three or four actions a day in the early spring months. He has a tendency to stoop forward and when tired falls down on all-fours.

Physical Examination.—A fairly well nourished but small boy, mentality low for his age, pupils moderately dilated, but not as much as they were in June. Patellar reflexes aggravated. Not mentally depressed. Sometimes plays as other children do, and again is unusually quiet.

Figs. 6 and 7 show the extent of the eruption. Additional illustrations, Figs. 8 and 9, are also given in order to show the various phases of the pellagrous eruption on the exposed portion of the body.

CASE IV.—Miss C. C. S., aged 25, white woman. Aunt on mother's side had nervous spells. Family history otherwise negative.

Previous good health. Was taken sick in March 1904. First symptoms were indigestion, diarrhœa and burning pain in stomach and "smothering feeling." Could not look at water or hear it splash, as it would make her very nervous, blind and dizzy, and

cause her to have shortness of breath. Was very thirsty, but was almost prohibited from drinking by the sensation produced by the sight of water, and only when thirst could be endured no longer would she force herself to swallow a few mouthfuls. Mouth was very red and sore, with quantities of thick saliva.

Eruption came on hands and arms two months after onset of diarrhoea, and one month later came on freely. These symptoms continued until September, when improvement set in and she thought she was well.

In spring of 1905 there was a repetition of all the symptoms, but more severe; well during winter. In spring of 1906, light attack, except mental depression was more pronounced.

These exacerbations and remissions have occurred each year since. In 1907 the diarrhoea was more severe than at any other period of the disease, the bowels acting as often as twenty times a day, for days at a time.

March 1908 all symptoms returned, eruptions being more extensive than any previous attack. Mental depression marked, vertigo severe. Has a desire "to run and go away hundreds of miles." Would be unable to sleep at night, and would get up and walk around the house for hours and not stop until forced to do so from exhaustion. Seen by me July 16, 1908.

Examination.—Emaciated woman, apparently 35 years old. Heart and lungs normal, abdomen negative, except for slight meteorism. Radial arteries palpable. Pellagrous eruption on hands, arms, elbows, and below elbows, neck, face, and chest. The extensive distribution in this case was due to her wearing a very thin shirt waist; although extensive, the eruption was symmetrical. Tongue a cardinal red and bald, abundance of thick saliva. Pupils widely dilated, reflexes exaggerated, marked tenderness in mid-dorsal region. Answers questions intelligently and promptly. She was advised to give up all products of corn in diet. No medicine prescribed.

Was seen in May, 1909, was then the picture of health and has gained 25 pounds. Bland's pills with atoxyl prescribed. On May 20, a slight diarrhoea set in and two weeks later the eruption appeared.

The following report was received from her September 29.

Entirely free of eruption, disappeared two weeks ago; has been very slight this year. Has kept out of sun; every time she went out the eruption would come back. Bowels have not been loose, rather constipated. Mouth has been very sore, as though burnt with lye. Troubled with sleeplessness, complains of her stomach and feeling weak, though for the last two weeks this has been relieved to a great extent. Some months ago had a very profuse "flow" lasting three weeks—almost a hemorrhage.

THE TREATMENT OF PELLAGRA

BY JAMES M. KING, B.S., M.D.

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BEFORE taking up the subject of the treatment of pellagra I think the question of prophylaxis should be mentioned. Foods consisting of cornmeal, or any of the ordinary products of corn, should be selected with great care. Corn containing rotten or moulded grains should not be made into food products, and only the best, well-ripened and dried corn should be used for meal, grits, etc. Corn-bread, grits, mush, and foods made from corn products should be thoroughly cooked and should be eaten while fresh. Corn products should be excluded from the diet of a pellagrous patient.

A patient suffering from pellagra should, to a certain extent, be quarantined or separated from close association with other members of the family, and I believe that the room, bedclothing, and vessels should be disinfected; for it is a fact that husband and wife have had the disease, one apparently following the other. It is also stated on good authority that one family who moved into a dwelling after another family that had suffered from pellagra contracted the disease. I think at least there would be nothing lost with the practice of ordinary care in respect to quarantine and segregation.

While I shall not go, by any means, into the details of diagnosis, I think it should be urged that every practitioner should keep this disease in mind and that as early a diagnosis as possible should be made. The typical skin eruption on the exposed surfaces is shown in the illustrations, Fig. 1 representing two brothers with the dermatitis especially marked on the lower legs; Fig. 2 shows a similar involvement of the face, arms, and hands. Recently I saw one case in which the first symptoms of pellagra appeared as a uterine hemorrhage which lasted for three or four weeks and was followed by severe diarrhœa and stomatitis, when finally a peculiar, dusky, brownish-red discoloration of the skin appeared

on the backs of the hands and knuckles of the fingers. Any condition of the uterus, vagina, the intestinal tract, or the mouth, which does not conform to the symptoms of any other disease, should be at once regarded as suspicious with respect to pellagra.

With reference to the treatment, I shall consider first the method of handling the skin manifestations. The erythematous type requires only cleanliness and applications of boric acid lotion, but if the blebs develop on the face, neck, or back of the hands and feet, more extensive treatment is demanded. The blebs should be punctured and drained, the surface should be washed with green soap and warm water once a day, sponged with boric acid lotion and an ointment consisting of boric acid, 8 gr.; zinc oxide, 1 dr.; lanolin and vaseline equal parts, to make one ounce. The ointment should be spread on rather profusely and the parts bound up, and the dressing should be made once or twice a day, depending upon the severity of the case. I have found this method of treatment to agree with the skin lesions better than any I have tried.

If the patient is up and going about, a general tub bath with soap and water, followed with a salt rub should be given daily. In some cases a cold spinal douche for stimulation may be of benefit. If the patient is bed-ridden, a cleansing soap sponge should be given daily, followed by a salt rub.

The question of internal treatment is a difficult one to deal with. The real cause of the disease not being known, we can only resort to general tonic treatment with special medication for the diarrhoea, irritable stomach, and stomatitis, should they arise. As a general tonic I have used arsenic, usually Fowler's solution, in tonic doses of from 3 to 5 drops after meals, and in conjunction with this I would suggest the use of iron, quinine, and strychnine when the stomach is not too irritable to receive such doses. If there is vomiting a tonic should be kept up, such as a solution of the peptonate of iron and manganese, with arsenic. In all cases sodium chloride should be given internally, 15 or 20 grains three or four times a day in water. Donovan's solution is an excellent tonic that may be used in some cases. I believe good has followed the use of tablets of lactic acid bacilli.

In all cases full nourishment of the patient should be urged. The food should be abundant, nutritious and well prepared.

Stomatitis, gastritis, and diarrhoea usually come together. Sometimes there is frequent vomiting with a severe diarrhoea, apparently uncontrollable, and a great deal of salivation. The skill of the physician is put to a test in this type of case. The mouth should be washed two or three times a day with a solution of peroxide of hydrogen, diluted with an equal part of water, and in addition to this an antiseptic solution like liquor antisepticus should be used after the peroxide of hydrogen. I have seen good results from the local application of the solution of silver nitrate to the ulcerations on the mucous membrane and tongue. A suitable solution to use is 15 grains of silver nitrate with glycerin and water equal parts to make an ounce.

The next point to look to is the irritable stomach, and I have used a mixture containing carbolic acid, bismuth subnitrate, and various digestants with some degree of success.

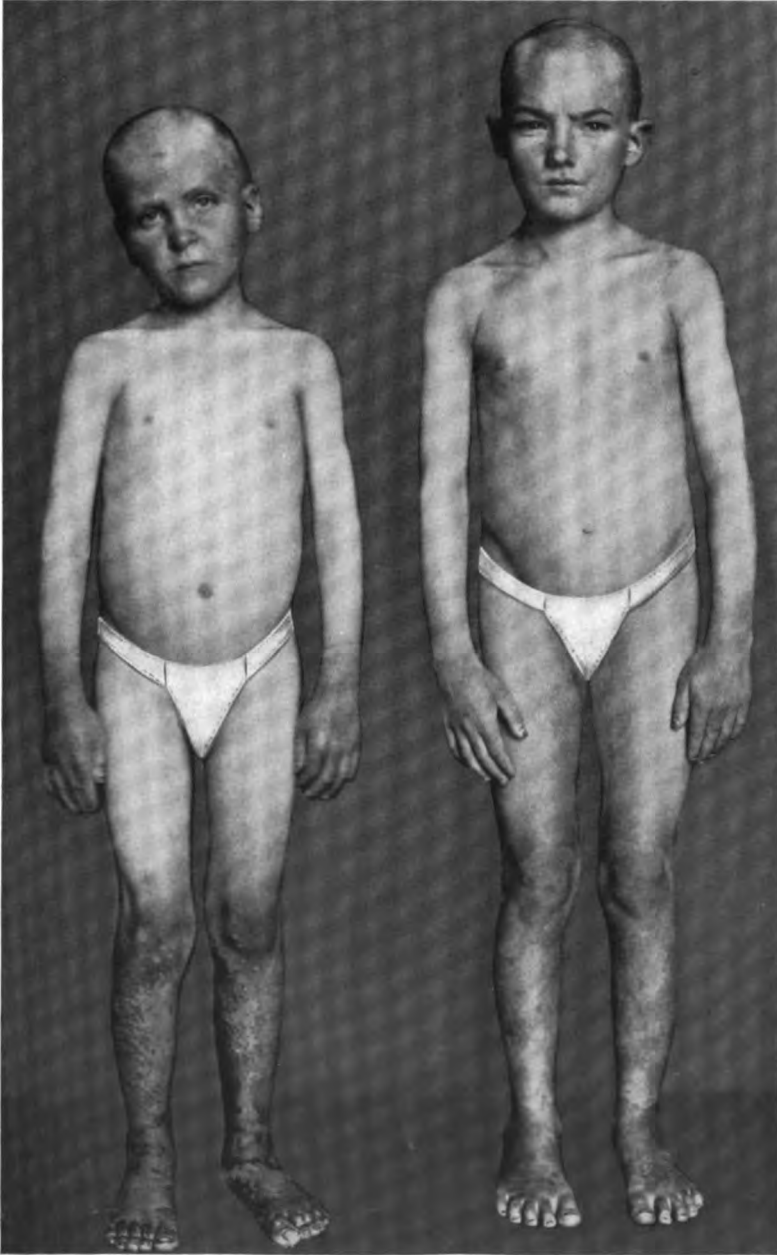
For the diarrhoea, pulverized opium with the acetate of lead may be used. Salol and bismuth in full doses often repeated may be of some service, but of all the difficulties met with in the treatment of pellagra, the diarrhoea is the hardest to control. It seems that all efforts are futile, though I have seen some patients with this uncontrollable diarrhoea, bed-ridden and apparently in the last stages of the disease, recover sufficiently to get up and look apparently well. During the severe stages of this condition a liquid diet should be given, and even rectal feeding may be resorted to. I have had patients, though suffering from the stomatitis, irritable stomach, and severe diarrhoea, take and retain well prepared milk toast served hot.

Sometimes a severe conjunctivitis develops. The ordinary methods of treatment for this condition should be followed. If corneal ulcers should develop, powdered calomel should be dusted into the ulcers and the eyes kept clean with boric acid lotion.

In case melancholia should develop later on in the disease, the bromides should be used. For insomnia veronal or trional, or better, a combination of the two should be given.

Fresh air should be allowed in abundance to every patient. Even if bed-ridden, the room should be fresh. If the patient is up and moving around, he should be required to stay in the open air most of the time.

FIG. 1.



**Pellagra eruption most marked on lower part of legs. Hands and face also affected.
(The smaller boy died during the summer of 1909.)**

FIG. 2.



Pellagra, showing the dermatitis of areas not protected by clothing. The eruption also appeared on the feet. (The patient died during the summer of 1909 in his second attack.)

FIG. 3.



Pellagra of hands and arms in acute active stage. The face, mouth, and tongue are also involved.

FIG. 4.



Pellagra of hand, showing a larger degree of amplification than in Fig. 3. There was no eruption on the palm.

FIG. 5.



Pellagra of feet.

In the treatment of the disease transfusion of blood has been resorted to, but with comparatively little success.

Atoxyl has been used but with no decided benefit over the other arsenical preparations.

The fæces of all cases should be subjected to a microscopical examination.

The illustrations (Figs. 1 to 5) show the lesions of pellagra in a satisfactory manner. It will be noticed that the dermatitis appears chiefly on the exposed portions of the body.

THE TUBERCULINS AND THEIR DIAGNOSTIC AND THERAPEUTIC USE *

BY JOHN BENJAMIN NICHOLS, M.D.

WASHINGTON, D. C.

THE introduction of tuberculin by Koch in 1890 aroused intense interest in the medical world, and great hopes were entertained of its therapeutic efficiency. These hopes were quickly overthrown, and it was soon found that in the doses then used tuberculin was a harmful and dangerous agent. Its employment for therapeutic and even diagnostic purposes, except in veterinary practice, was practically abandoned for many years. Within the past few years, however, largely under the influence of Sir Almoth E. Wright and Edward L. Trudeau, the use of tuberculin has been revived.

THE TUBERCULINS

A number of different preparations termed tuberculin are in use, ordinarily designated by letters which seem cabalistic and mysterious to the uninformed, but which indicate radical differences in preparation, action, and dosage. The different kinds of tuberculin must be employed with the greatest discrimination and care, as what would be a proper dose and clinical use for one kind would be homicidal for another. I have therefore entitled this paper, not "Tuberculin," but "The Tuberculins." The tuberculins are either extracts of the soluble constituents or products of growth of tubercle bacilli, or are suspensions of the insoluble components of these bacilli. It may be noted, therefore, that tuberculin, as the term is now generally used, is not in any true sense a *serum*, that is, the blood-serum from an inoculated or otherwise treated animal.

The tubercle bacilli used in the preparation of tuberculin are obtained by growing the strains in flasks of glycerin bouillon for several weeks. At the end of this time the bacilli form a large

* Read before the Clinical Society of the District of Columbia, Oct. 11, 1909.

matted mass on the surface of the medium, and may be separated by filtration. Either the bacillary mass or the filtered culture fluid is used for the preparation of the tuberculin desired.

A large number of tuberculin preparations have been introduced; the chief varieties now in use, and the main types of these products, are as follows:

Tuberculin O.—This variety, ordinarily called “old tuberculin,” is essentially the preparation originally introduced by Koch, and is official in the German Pharmacopœia of 1900 under the designation *Tuberculinum Kochi*. The letters “T.O.” are ordinarily taken to signify Tuberculin “Old,” or “Original”; but have also been used to signify Tuberculin Oberer, referring to the clear supernatant fluid after sedimentation of a tubercle-bacillus culture. In Germany and France the designation “T.A.” is used, meaning Tuberculin Alt or Tuberculin Ancien.

This preparation is made by growing tubercle bacilli in glycerin bouillon for six weeks or more; sterilizing the culture by heat (as by the autoclave); evaporating at a temperature approaching 100° C. until reduced to one-tenth of the original volume; and finally filtering. The filtrate constitutes “T.O.,” and consists of a thick, clear, straw-colored fluid containing, besides the specific principles, about 40 to 50 per cent. of glycerin, and the concentrated constituents of the original bouillon.

It will be seen that “T.O.” is a glycerin-aqueous extract or solution of the soluble products of the growth of tubercle bacilli and of the extractible soluble constituents of the bacilli themselves; all exposed to heat (approximating 100° C.) for a prolonged period, sometimes for two days.

“T.O.” is used for both diagnostic and therapeutic purposes; its hypodermic dose for diagnostic purposes being 0.25 to 10 mgm., for therapeutic use 0.001 mgm. up (according to the patient's tolerance) toward 1 c.c.

Purified or precipitated tuberculin is prepared by precipitating “T.O.” with alcohol, and washing and redissolving the precipitate in salt solution in any strength desired. It is now used mainly for the ocular diagnostic test.

Tuberculin Bouillon Filtrate, “B.F.”—This is the filtrate obtained by passing a bouillon culture of tubercle bacilli through a

porcelain or germ-proof filter. The fluid is used unconcentrated and is not subjected to heating, freedom from the bacilli being effected by the filter and assured by animal inoculation. This preparation is therefore a solution in glycerin-bouillon of the soluble products of growth of the tubercle bacillus, without any changes being brought about by heat. It is used therapeutically, in the same doses as "T.O." It is often called Denys's tuberculin, but the form was really used in the early work of Koch, and is sometimes styled Tuberculin-Original-Alt ("T.O.A.").

A preparation of "B.F." concentrated to one-tenth by evaporation, without heat, in a vacuum has been introduced,—“Vacuum Tuberculin.” It corresponds in concentration to “T.O.”

Tuberculin Rest, Rückstand, or Residue, "T.R."—This was introduced by Koch in 1897, and is one of the varieties sometimes called “new tuberculin.” In its preparation, a mass of tubercle bacilli is dried, ground, treated with salt solution, and centrifugated. The supernatant fluid (“T.O.”), containing the extracted soluble constituents of the bacillary mass, is discarded, and from the sediment (the “Rest” or “Rückstand,” or washed solid remains of the bacilli) is prepared the “T.R.” The Rückstand, by a process that need not be described here, is finely comminuted and worked into a fine emulsion or suspension in salt solution, to which is added 20 per cent. of glycerin, and the whole is sterilized by heating at 60° C. for an hour or more. The product is so standardized that 1 c.c. of “T.R.” contains 2 mgm. (0.2 per cent.) of dried bacillary substance, coming from 10 initial mgm. of tubercle bacilli; that is, 1 Gm. of dry bacilli to begin with makes 100 c.c. of “T.R.”, which in its final form, however, contains only 0.2 Gm. of dry bacillary substance, the remaining four-fifths of the original bacilli being lost in the process. This tuberculin is an opalescent fluid, containing, besides the specific principles, 20 per cent. of glycerin, NaCl, etc.

It will be seen that “T.R.” represents solely the insoluble constituents of the bodies of tubercle bacilli, as contrasted with the old tuberculins, which represent solely the soluble products and constituents of the organisms.

This preparation is used therapeutically. There has been some confusion in expressing the dosage—some understanding the dose to refer to the whole fluid, others to the amount of initial bacillary

substance used, still others to the dry solids in the final product. Thus, a dose of 0.001 mgm., if it meant of the final dry solids, would constitute 0.5 mgm. of the fluid tuberculin, and represent 0.005 mgm. of the original bacilli. In practice, this matter of dosage should be clearly understood, as the dose wet is 500 times the dose dry, and a mistake of this magnitude in administration would result either in enormous and harmful over-dosage or in infinitesimal and ineffective under-dosage. This discrepancy in the statement of dose is seemingly not understood even by some of the manufacturers and dealers in tuberculin. Wright and many others express dosage in terms of final dry residue—that is, a given dose means enough of the tuberculin if dried to yield that weight of dry bacillary solids. This is the method of stating dosage which I personally use.

The dose of "T.R." (as used by Wright) is from 0.00005 mgm. to 0.0025 mgm. of the dry solids.

Tuberculin Bacillen (or Bacillus) Emulsion, "B.E."—This is another "new tuberculin," introduced by Koch in 1901. It consists of thoroughly ground and dried tubercle bacilli suspended in equal parts of 0.8 per cent. NaCl solution and glycerin, of such strength that 1 c.c. of the preparation contains 5 mgm. (0.5 per cent.) of dry bacillary substance. It is sterilized by heating at 60° C. for one to five hours. It represents the entire bacillary substance, the soluble as well as the insoluble portion, and is analogous to Wright's bacterial vaccines in general. Its use is therapeutic, and the dose is from 0.00005 mgm. to about 0.0025 mgm. of dry bacillary substance. Similar confusion as to dosage obtains with this as with "T.R." It is a thick cloudy or milky fluid.

The foregoing tuberculins are ordinarily made with the human variety of the tubercle bacillus. Tuberculins are also prepared from the bovine variety of the bacillus, this line of preparations being sometimes termed "Perlsucht Tuberculins" ("P.T."), of which the same products may be had as of the human variety, namely, "P.T.O.", "P.T.B.F.", "P.T.R.", and "P.T.B.E."

The tuberculins can be divided into two distinct classes, which may be designated the *old tuberculins* and the *new tuberculins*. The old tuberculins ("T.O." and "B.F.") contain exclusively the soluble products of growth and soluble constituents of the substance

of tubercle bacilli; the new tuberculins contain the insoluble constituents of tubercle bacilli, the "T.R." exclusively, the "B.E." all the constituents, soluble and insoluble, of the bacillary bodies. Corresponding to these two classes are fundamental differences in therapeutic use which will be considered presently.

The tuberculins are marketed in small vials (1 c.c., etc.), and in this stock form containing (except "B.F.") from 20 to 50 per cent. of glycerin, are believed to retain their strength indefinitely. They should be kept cool and in the dark.

For hypodermic administration it is necessary to dilute the stock tuberculin to a manageable volume. Old tuberculin can be diluted with an aqueous solution of 0.85 per cent. of NaCl with 0.25 per cent. of phenol or liquor cresolis compositus (lysol); dilutions containing 0.01 mgm., 0.1 mgm., 1 mgm., and 10 mgm. of "T.O." per c.c. being convenient for use. With the new tuberculins, the bacillary material is apt to agglutinate in dilutions with simple salt solution, and for these the soft soap in 0.25 per cent. lysolized 0.85 per cent. NaCl solution will aid in maintaining a homogeneous suspension; 20 per cent. glycerin solution is also recommended for diluting new tuberculin. A convenient strength of dilutions of "T.R." and "B.E." is 0.001 mgm. and 0.01 mgm. per c.c. Serial dilutions of tuberculin are marketed already prepared. Tuberculin dilutions are claimed by the dealers to retain their efficiency only for a few weeks; but I have found dilutions of "T.O." potent after 9 months.

DIAGNOSTIC USE OF TUBERCULIN

There are three general methods of employing tuberculin for diagnostic purposes, namely, the subcutaneous, the cutaneous, and the ocular tests. For all of these "T.O." or some derivative therefrom is used, also occasionally "B.F."

Subcutaneous Tuberculin Test.—This is performed by making a hypodermic injection of "T.O.", in doses of from 0.25 to 10 mgm., and observing the results. In non-tuberculous subjects there is ordinarily no reaction, even in many cases after doses of as high as 50 mgm. In tuberculous subjects a characteristic series of reactive phenomena ordinarily follows the injection, beginning in a few hours, attaining a maximum in 12 to 36 hours, and disappearing

in 2 or 3 days. These phenomena are divisible into three groups,—local, focal, and constitutional.

The local reaction consists in the development of a varying amount of swelling, induration, tenderness, and redness at the site of injection. Usually this is trifling and insignificant, but occasionally it is well-marked, and in rare instances a severe cellulitis occurs, with the area greatly swollen, indurated, inflamed, and exquisitely painful, looking like an angry and threatening case of cellulitis, which, however, subsides in a few days without proceeding to suppuration (see *Frontispiece*).

The focal reaction consists in an exacerbation of disease activity at the site of the tuberculous lesions. At the foci of disease in the lungs, for instance, there may be changes in the breath sounds and an increase of râles, with an augmentation of expectoration and cough. An increase of ulceration may bring on some hæmoptysis. With a tuberculous cystitis there may be increased dysuria. In surface lesions the increased inflammatory action is visible to the eye. A distinct focal reaction is a most important diagnostic sign.

The constitutional reaction consists in the appearance or aggravation of systemic symptoms, such as malaise, prostration, headache, pains in joints, anorexia, nausea and vomiting, and especially fever. As the temperature is susceptible of exact measurement and is so characteristically affected in tuberculous subjects, it is usually taken as the main criterion in the subcutaneous tuberculin test.

There are certain contraindications to the subcutaneous injection of such large amounts of tuberculin as are required for diagnostic purposes. Patients in active stages of the disease are unsuitable subjects, owing to the manifest inadvisability of still further increasing the disease processes or of taking the risk of lighting up dormant lesions. Recent or recurring hæmoptysis is an especial contraindication, owing to the hazard of inciting fresh hemorrhage. The undesirability of excessive focal reactions is obvious. Fever is a contraindication, not only because it indicates the existence of too great disease activity, but also because the fluctuations of temperature obscure the febrile rise which is an essential feature of the test.

In suspected cases, in which there is no fever and the symptoms are dormant, sluggish, or incipient, the test is suitable and may be

carried out thus: For two or more days prior to the test the temperature and pulse are taken at frequent intervals,—every two hours if possible, or certainly four times a day. If this record shows a normal temperature 0.25 to 0.35 mgm. of "T.O." is injected subcutaneously in any convenient locality, and the temperature record and clinical observation continued for three or four days. If no reaction occurs, the test is repeated, using 2 to 4 mgm. If the result is still negative further injections of up to 6 to 10 mgm. may be given. If practicable, a larger number of injections may be given, with a more gradual increase in the dosage, though the possibility of thus producing artificial sensitization should be borne in mind. All the clinical phenomena following the injections should be carefully observed, and due weight given to the local, focal, and constitutional symptoms as well as to the temperature. A rise of temperature of 1° F. or more over the maximum during the preliminary observation period is regarded as conclusive. The temperature rise usually takes place during the first 24 hours after the injection, but is occasionally delayed to the second 24 hours. Even in the absence of a febrile reaction the other symptoms, and especially the focal reaction, may be diagnostic.

Cutaneous Tuberculin Test.—This test depends on the local reaction produced by the introduction of "T.O." into the skin; and as the reaction is superficial and innocuous the test is available for any subject whether fever and active disease processes are present or not. There are two main methods of performing the test, the scarification method of Von Pirquet and the inunction method of Moro, introduced in 1907 and 1908 respectively.

The method of Von Pirquet is essentially the same as that of vaccinating against smallpox. For scarifying, a needle point, scalpel, or special instrument may be used, while for inoculation "T.O." is employed either in full strength or in various dilutions. Much use has been made of 25 per cent. dilutions (with NaCl solution), while Von Pirquet at the present time, it is understood, uses the full strength "T.O."

Von Pirquet's own method is about as follows: A minute drop of the tuberculin used is placed on the cleaned skin (say of the arm) at two points 3 inches apart, and midway between them a drop of control solution similar in composition (especially in glycerin con-

tent) to the menstruum containing the tuberculin. The point of a special drill-like scarifier is then placed against the skin through each drop and the instrument twirled with sufficient pressure to cause a slight abrasion of the epidermis and open up the lymph-channels, without necessarily drawing blood. Care should be taken that no tuberculin is carried over into the control. The skin is allowed to dry a few minutes, and the parts kept under observation for a few days. If the result is negative the control and inoculated areas will be unaffected, or affected but slightly and equally. If the result is positive the control will show no change, while the inoculated points will become surrounded by a hyperæmic zone 5 to 30 mm. in diameter, with slight swelling, induration, and papulation of the skin. This appears in a few hours, is at its height in 24 to 36 hours, and then in the course of 2 or 3 days subsides and disappears. The reaction varies in intensity and duration in different cases (see *Frontispiece*).

Detre in 1908 introduced a differential cutaneous test, vaccinating with tuberculins of both human and bovine type, and claimed from the relative intensity of the two reactions to be able to determine the type and stage of the infection. His claims have not been substantiated.

For Moro's test a tuberculin ointment composed of equal parts of "T.O." and anhydrous lanolin is used. About 0.1 Gm. of this ointment is vigorously rubbed for $\frac{1}{2}$ to 1 minute over an area of 3 or 4 square inches into the skin of the abdomen or mammary region. If a positive result follows there appear within 10 to 36 hours at and near the place of application a varying number (sometimes over a hundred) of small red papules, which in the severer reactions are surrounded by hyperæmic areas and accompanied by itching (see *Frontispiece*).

Another method of performing the cutaneous test is that of Lautier, which consists in applying to the skin for 2 or 3 days a pledget of cotton saturated with 2 or 3 drops of a 1 per cent. dilution of "T.O." held in place under an impervious cover. A positive reaction consists in the appearance of vesico-papules.

Ocular Tuberculin Test.—This test was developed independently in 1907 by Wolff-Eisner, and Calmette. It can be used in patients with fever and active lesions, but should not be applied in cases

where there is any inflammation of the conjunctiva or eye structures. For the test Wolff-Eisner and others have used a 1 to 5 per cent. dilution of "T.O."; Calmette a 0.5 to 2 per cent. solution of purified or precipitated tuberculin (washed alcoholic precipitate from "T.O."). It should be noted that these solutions of precipitated tuberculin are about ten times as strong as the corresponding dilutions of "T.O." Tablets of dried tuberculin substance have also been put on the market for the ocular test, to be dissolved in water at the time of use. Apparently 1 to 5 per cent. dilutions of "T.O." with 0.85 per cent. NaCl solution are quite suitable for this test.

To perform the test, the eyes are inspected, and if the conjunctivæ are normal and alike in appearance, a drop of a tuberculin dilution, say a 1 per cent., is instilled into one eye. The development of congestion or inflammation of the conjunctiva of the inoculated eye,—redness, exudation, sandy feeling, etc.,—within 12 to 36 hours, and lasting for 2 or 3 days, constitutes a positive reaction; comparison is made with the uninoculated eye, which serves as a control. If no reaction occurs a drop of a stronger dilution (say a 5 per cent.) may be instilled into the other eye and the result observed. At times a severe conjunctivitis is set up.

Tuberculin tests on other mucous membranes besides that of the eye have been performed, as in the urethra, or on the side of the frænum linguæ.

What value is to be attached to the occurrence or non-occurrence of a reaction after the different tests with tuberculin? In veterinary practice the occurrence of a febrile rise (of at least 2° F., and up to about 104°) after a subcutaneous injection of tuberculin is taken as practical proof of the existence of tuberculosis. The discrepancy between the inoculation results and autopsy findings in cattle in large series of observations is under 3 per cent.

In human practice the diagnostic interpretation of tuberculin tests cannot be given such positive value as in veterinary practice.

Negative Reactions.—In the first place, in some advanced cases of tuberculosis no reaction to tuberculin occurs, the disease process apparently having overwhelmed the defensive resistance. As in such instances the diagnosis is ordinarily obvious from the other clinical manifestations, these exceptional cases do not greatly interfere with the diagnostic usefulness of tuberculin, which

is of most utility in early and doubtful cases. Aside from these exceptions, a negative tuberculin test, adequately applied, may be taken as practical evidence that the subject has no active tuberculous lesion.

Positive Reactions.—On the other hand, the reaction is positive not only in those with active tuberculous manifestations, but also in many of those who have previously had tuberculous lesions, even very insignificant ones, but which are completely healed and cured. The test is too delicate, not differentiating between clinical tuberculosis and cured tuberculosis. As the great majority of people are believed to have healed tuberculous foci, many subjects give a tuberculin reaction who practically at the time have no tuberculosis. For example, in tests on large numbers of hospital patients positive tuberculin reactions occurred in about 50 per cent. of those who presented no other evidence or suspicion of tuberculosis. In children, the proportion of clinically non-tuberculous cases reacting diminishes with the age, thus paralleling the increasing incidence of slight and unsuspected tuberculous foci as age advances. A positive tuberculin reaction is therefore not clinically and practically of absolute or pathognomonic value. It is often of real diagnostic usefulness, but must be considered and interpreted only in connection with all the other clinical manifestations in the case.

As to the comparative results and choice of the three main methods of tuberculin testing, subcutaneous, cutaneous, and ocular, sometimes in the same subject a reaction will occur after one and not after another. The subcutaneous and cutaneous tests are said to give the most closely parallel results, while the ocular reaction is least sensitive and fails more often when the other methods are positive.

The advantage claimed for the ocular test is that, from its less sensitiveness, positive results are confined more closely to cases with active tuberculous lesions; but it fails in some manifestly tuberculous cases. The danger of occasional excessive inflammatory reactions has apparently recently brought it into some disfavor. In my own limited experience with it the difference between the inoculated and uninoculated eyes that constitutes a positive reaction was often so slight that it seemed of little reliability for diagnosis.

The cutaneous test of Von Pirquet is regarded as excessively sensitive, especially in adults, reacting in many cured cases. In young children its indications are more reliable. Its simplicity and harmlessness, and its availability in febrile and active cases, recommend its trial, the diagnostic limitations being strictly borne in mind.

Personally I have felt that the subcutaneous test, in the cases adapted to its use, is the preferable one, although it too is of excessive sensitiveness and is not free from danger of severe reactions. I am accustomed to give two injections, the first of 0.25 or 0.35 mgm., the second of 3 or 4 mgm. One advantage of this test is that a distinct focal reaction may be taken as positive proof of the existence and location of active tuberculous lesions.

In general, in the diagnostic use of tuberculin no set rules as to technic or interpretation can be laid down. Each case must be individualized as to the use, the method of application, and the dosage of tuberculin; and the results obtained are to be interpreted only in the light of the entire clinical picture.

Phenomena of sensitization may be produced by the diagnostic use of tuberculin. One application of tuberculin to a conjunctiva of even a normal subject is apt to sensitize it so that a subsequent instillation into the same eye of an equal or even a less amount of tuberculin may produce a positive and even a violent reaction. It is a common occurrence for an ocular or cutaneous reaction to reappear when, subsequent to the local instillation, a subsequent hypodermic injection of tuberculin is given; these "return reactions" or "flarebacks" would seem really to belong to the class of focal reactions, the result of local sensitization. The possibility of constitutional sensitization after subcutaneous injections of tuberculin in diagnostic doses may also be borne in mind, as a reaction after such repeated injections might conceivably result from an artificial sensitization.

THERAPEUTIC USE OF TUBERCULIN

The disastrous results of the early attempts at tuberculin therapy created a strong prejudice and distrust of this agent, but by the methods in use at the present time it can be employed with perfect safety and with claimed advantage in many instances. It

is generally agreed that the cases best adapted to the treatment are the slow, inactive, non-febrile, localized, surgical cases of tuberculosis, while the cases not adapted to it are those in active stages, with marked constitutional toxic symptoms, and especially those with fever (say, with temperatures over 100° F.). Even in febrile cases, however, the treatment has been employed.

Final agreement as to the best method for the therapeutic administration of tuberculin has not been attained, but there have been developed two general methods, which for convenience may be designated as that of Wright and that of Trudeau.

Wright's method consists in the continued administration of small doses of new tuberculin at intervals determined by the opsonic index and clinical course of the case. The aim is to maintain the opsonic and other antibacterial powers of the blood at the most efficient level possible. The opsonic determination may be dispensed with and the symptoms followed as a guide to the dosage. Ordinarily, injections (hypodermic) are made every ten days of "T.R." or "B.E." in doses ranging from 0.00005 mgm. to 0.0002 mgm. initially, gradually increased to 0.001 mgm. or 0.002 mgm. If the patient does badly, the doses should be diminished or the injections made at longer intervals or suspended altogether. With these doses reactions are rare. The treatment may have to be kept up for months before results appear. This method has been mostly used for localized, surgical, and non-pulmonary cases of the disease, and many cases of cure or improvement under its use have been reported.

Trudeau's method consists in a more frequent hypodermic administration of tuberculin, usually old tuberculin ("T.O." or "B.F."), beginning with small doses (0.001 mgm. to 0.01 mgm.) and gradually and cautiously increasing to the limit of the patient's tolerance, in some instances as high as 1 c.c. The injections are usually given about twice a week at first, with longer intervals as higher doses are reached. The course of treatment may require a year or more. Reactions (local, focal, and constitutional) are to be avoided so far as possible, effort being made to keep the dosage down to amounts not sufficient to cause marked reactions. An invariable rule is never to give an injection until all reactive phenomena from the preceding injection have subsided. When a

dose producing marked reactions has been reached, further increase of dose should be made very gradually and cautiously. The meeting of these indications, and the course of the case, will determine the frequency, the amount, and the rate of increase of the doses. Many cases can by this regime be habituated to a high degree of tolerance to relatively enormous doses of tuberculin, just as by a similar course the organism can become habituated to large doses of such poisons as morphine, etc. In this process the anaphylactic sensitization of the organism against the tubercle bacillus, which is by many regarded as a defensive agency, is broken down; but an immunity and tolerance to the toxic effects of the products of growth of the bacilli is established. However the mechanism of cure is accomplished by Trudeau's method, beneficial results are confidently claimed for it by many competent observers. It has been mainly used in pulmonary cases of tuberculosis.

We thus have presented for our choice two contrary methods of tuberculin therapy, sharply contrasting in essential particulars.

Trudeau's method employs old tuberculin, the soluble products and components of the bacilli, or soluble antigens, generating antibodies against the toxins of the disease; Wright's employs new tuberculins, the insoluble components of the bacillary substance, or insoluble antigens, generating antibodies against the bacilli themselves. One method is antitoxic, the other antibacterial. One inactivates the products of the growing bacilli, the other antagonizes the bacilli themselves. One is a process of habituation, the other of simple maintenance of the agencies of bacterial resistance. One overwhelms and destroys, the other maintains the body sensitiveness or anaphylaxis to tuberculin, which there is reason to regard as a defensive agency.

The relative merits of these two methods are undeterminable with our present knowledge; each has substantial support, in theory and in practical results; and in making a choice for use one must be influenced by his observation, his theoretical predilections, or whatever light is obtainable.

Hypersensitiveness is a condition that occasionally appears in both diagnostic and therapeutic work. By this is meant, after repeated injections, an increasing rather than decreasing sensitiveness in reacting to tuberculin; that is, the appearance of a reaction,

or a severer reaction, after a given dose of tuberculin when equal or greater doses previously have caused less reaction. The development of this condition is unfavorable, and necessitates suspension of the administration of tuberculin or its continuance with much diminished doses and with great caution.

Attempts have been made to administer tuberculin by the mouth or by rectum; but while the agent perhaps has some action when given in these ways, it cannot be doubted that subcutaneous administration is much the most efficient.

A consideration of the details of the physiological action of tuberculin, and of the processes that take place to constitute the reactions, cannot be entered upon at this time. These processes, indeed, have not yet been elucidated and are as yet in the realm of theory and speculation rather than of demonstrated fact.

In conclusion, the therapeutic use of tuberculin seems of promise in the treatment of suitable cases of tuberculosis. It does not interfere with other methods of treatment, no other therapeutic measures should be neglected during its use, and it is a useful auxiliary to other treatment. Great care must be exercised in its use, the cases must be individualized, and the patients kept under vigilant observation. There is a natural temptation or inclination to increase the doses too rapidly; this should be resisted, the small doses should be contentedly given, and the increases made slowly and gradually. The danger of over-dosage cannot be too strongly borne in mind; the evil effects may be insidious in development, but difficult to control when once incited. When patients are doing badly tuberculin must be used cautiously or discontinued altogether. Too marked or immediate results should not be expected; months of treatment are often necessary before perceptible results are obtained. In many cases there may be no improvement at all from the treatment; but the benefits that are obtained in other cases make the method worth trying under suitable conditions.

Medicine

SOME RECENT ADDITIONS TO OUR KNOWLEDGE OF PURIN METABOLISM AND THEIR BEARING ON THE PROBLEMS OF GOUT

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THE progress which has been made during the last few years in our search into the tangled mazes of intermediary metabolism has come, more than from any other source, from a recognition of the fact that every step of metabolism, no matter how simple or how complex, is brought about by the action of intracellular enzymes, and that these enzymes are highly specific, widely distributed, but not always distributed alike in different species of animals or in different tissues of a single species. Consequently, in the numerous changes which take place in each and every sort of foodstuff between its absorption from the bowel and the excretion of the fragments into which it is burned or disintegrated, many different enzymes are concerned—far more than we formerly suspected. Furthermore, each of these enzymes has its own particular distribution, its own particular field of action, and this action is modified, inhibited, or accelerated by various and sundry antibodies, accelerators, activators, and inhibitors, some of which are specific and some of which are not; and also, some of the enzyme reactions seem to be reversible, while with others reversibility cannot be demonstrated under experimental conditions. And so we find that the more light we let into this metabolism tangle the deeper we find it to be, and the hope of unravelling it would grow dim were it not for the sense of progress that we have from getting in thus far.

Thanks to the existence of reasonably reliable methods for quantitative analysis, it has been possible to follow out the changes

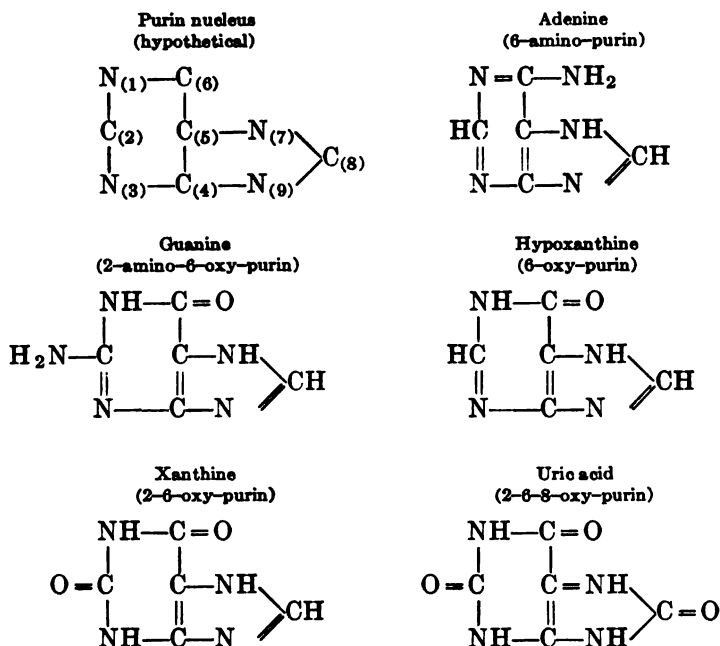
that take place in the metabolism of the purins somewhat farther and better than we have so far done with many of the other food and tissue compounds, and the results of this work illustrate what we may expect to meet with in other studies of metabolism.

DECOMPOSITIONS OF NUCLEO-PROTEINS

It will be recalled that while the purins are the best known and most characteristic constituents of the all-important nucleoproteins, yet they constitute but one of several groups which make up this complex molecule. And so, even if we do finally follow out completely the steps of purin metabolism, a feat which is still far from being accomplished, we shall have worked out but a small part of the catabolism of the nucleins. The nucleins are, it will be remembered, compounds of protein with nucleic acid, and the nucleic acid is itself composed of a complex organization of carbohydrates, purins and pyrimidines, held together by phosphoric acid radicals. With such a heterogenous structure the possibilities for variety in the nucleoproteins would seem to be unlimited, and so it is not surprising to find that they are regarded as among the most specific of the cellular constituents, differing in some characteristic way in even closely related structures and organs. On the other hand, recent work indicates that the nucleic acids of different organs are themselves similar or identical (Jones²⁵), and the situation regarding the purins of the nucleoproteins seems to be perhaps a little less complex than we at one time believed, for which steps towards simplification we should be grateful, since nearly every other development has been towards complexity. Of the five purins which are known to occur normally in the tissues or fluids of mammals, namely adenine, guanine, hypoxanthine, xanthine, and uric acid, only the first two seem to exist in the cellular nucleins, the other three being derived from the adenine and guanine during the processes of metabolism. The relationship which exists between these substances is understood better after inspection of their structural formulæ (page 78) than it could be after the most exhaustive verbal description.

It can be readily seen by inspection of these formulæ that the changes which must take place to produce the uric acid of the urine from the nucleoproteins of the food and tissues, are essen-

tially of three different sorts—first, a cleavage of the nucleo-proteins and liberation of the adenine and guanine; second, removal of NH_2 groups from these two amino-purins; third, addition of oxy-
gen to produce the oxy-purin uric acid. These changes are accomplished by specific enzymes in a series of steps, each of which is now known, thanks especially to the labors of Schittenhelm, Walter Jones, and their collaborators.



The first step consists of the liberation of the nucleic acid from the protein with which it is bound, and this process seems to be accomplished by any of the several enzymes which digest proteins, including not only trypsin, but also the intracellular autolytic enzymes. The process seems to consist essentially of a digesting away of the protein, leaving the nucleic acid free. Therefore in intestinal digestion of nucleoproteins the nucleic acid is set free by trypsin before absorption, to be further acted upon by the intestinal juice and the intestinal wall.^{33 34} It is of interest to consider that a similar process seems to take place within the tissues under both physiological and pathological processes. Thus

in the disintegrative processes of anæmic necrosis of tissues, the disappearance of the nucleus is preceded by a stage in which the nucleus appears small, but staining with unusual intensity by basic dyes; this condition, commonly referred to as pycnosis, probably depends upon the liberation of the nucleic acid from the basic protein substances with which it has been combined, thus permitting it to unite with a greater amount of the basic dye.²³ Likewise in germinating cells we find an intense affinity for basic dyes exhibited by the nuclear material, which is also probably due to liberation of nucleic acid by intracellular enzymes, for it is known that germinating cells, such as spermatozoa, contain large amounts of free nucleic acid. Here the cleavage of nucleoprotein seems to be a physiological process, and a part of cell multiplication which is accomplished by enzyme action.

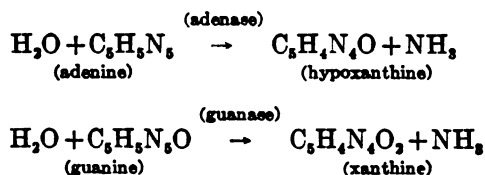
After the nucleic acid has been isolated, however, it cannot be further attacked by the proteolytic enzymes, since it contains no protein constituents, and its further disintegration is accomplished by a distinctly different enzyme (Sachs²⁴), the *nuclease*, as it has been appropriately designated. This enzyme seems to act specifically on nucleic acid. Corresponding to the universal presence of nucleic acid in every cell, no matter of what kind, nuclease seems to have an equally universal distribution, and no tissue or cell has yet been found which did not possess the power of liberating purins during autolysis; indeed one of the earliest observations of autolysis was that of Schützenberger, who, in 1874, found that free purins appeared during the selfdigestion of yeast. So, too, in the earliest stages of embryonic development nuclease is present.¹⁹

FORMATION OF URIC ACID

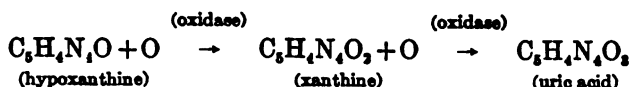
The nucleic acid upon its decomposition liberates adenine and guanine, and apparently always and only these two, no matter what the source of the nucleoprotein may have been.²⁵ Besides these purins there are also set free carbohydrates and pyrimidines, but the subsequent changes in the latter constituents have not yet been worked out as completely as those in the former. The two purins are attacked by deamidizing enzymes, that is, enzymes which possess the power of removing NH_2 groups from organic compounds. Such enzymes are undoubtedly of wide distribution and

great importance, deamidization being one of the most essential of all reactions in protein metabolism, since the amino-acids which compose the protein molecule all possess the NH_2 group, which must be split out and excreted as urea, leaving the rest of the molecule available for energy production through oxidation. Perhaps the most striking thing about the deamidizing enzymes which attack the purins is their remarkable specificity, for, closely related as guanine and adenine are, each requires a specific enzyme to accomplish its deamidization. This fact was shown by Jones and his co-workers,^{85 11} who found that extracts of the liver and the spleen of the pig can deamidize adenine but do not act upon guanine, while the pancreas and other organs will act upon both. Other cells, as, for instance, yeast cells, can deamidize guanine but not adenine.² Furthermore, it has been found that in the development of the human fœtus the power to deamidize guanine appears earlier than the power to deamidize adenine.¹⁶ If we look at the structural formulæ we see that the chief difference between adenine and guanine is the position at which the NH_2 group is attached to the purin ring, yet that difference is sufficient to require a different enzyme, indicating a specificity almost as striking as that existing in the enzymes which attack the sugars. In view of the existence of two distinct enzymes for the deamidization of the two purins, one must wonder if it will not eventually be found that there are distinct deamidizing enzymes for each and every one of the many amino-acids which are produced by cleavage of protein molecules.

Replacement of the amino-group in adenine and guanine by an oxygen atom changes them respectively into hypoxanthine and xanthine, as can be seen from the structural formulæ. Empirically expressed the reaction is as follows:



Next the hypoxanthine is oxidized to xanthine and then both to uric acid, according to the following equation:



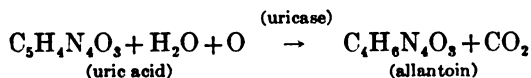
The enzyme that converts xanthine into uric acid, first called *xanthine-oxidase* by Burian,²⁷ is unequally distributed in different organs and species. For example, xanthine-oxidase is present in the spleen of the dog, horse and cow, but not in the spleen of man or of the pig; on the other hand, it is present in the liver of pig and man, but not in the liver of the dog. In the development of the pig and of man it is found that this enzyme does not appear until about the time of birth, in contrast with the early appearance of the adenase and guanase.^{19 16 26} Some of the simplest organisms, such as yeast² or a mollusk,²² seem not to acquire this oxidizing enzyme at all. As yet it has not been ascertained whether a separate enzyme changes the hypoxanthine into xanthine, or whether this reaction is accomplished by the xanthine-oxidase, but by analogy a separate enzyme might be expected, specific for this reaction, and certain unpublished results obtained by Corper and myself seem to support this view. For example, if a solution containing "xanthine-oxidase" acts upon hypoxanthine in a closed vessel without access to air the hypoxanthine slowly goes over into xanthine, and the xanthine does not change in appreciable amount to uric acid until a liberal supply of air is provided. Apparently the oxidation of hypoxanthine is accomplished under conditions which do not allow of the oxidation of xanthine, and this suggests that a different enzyme is concerned.⁴⁷ The action of xanthine-oxidase seems not to be reversible.²⁷

By these steps, as outlined above, uric acid is formed from the nucleoproteins and free purins of the food and tissues, through the action of several specific enzymes. Although in the bird and reptile uric acid can be synthesized in the tissues from simpler compounds, in mammals so far as we now know all uric acid is formed from the purins only, and apparently, only through the stages indicated. The following observation bearing upon the last point was made several years ago by Minkowski. If food rich in adenine is fed to dogs the adenine is excreted as uric acid or its decomposition product, allantoin. If, however, pure adenine (6-amino-purin) is fed to the same animal it is depos-

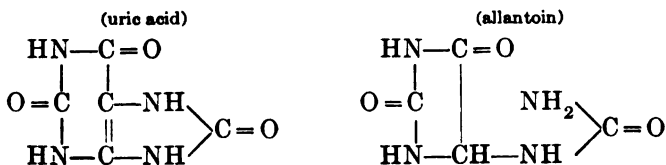
ited in the kidney, not as uric acid (2-6-8-oxy-purin), but, according to Nicolaier⁸⁷ as 2-8-oxy-6-amino-purin. In other words, artificially isolated adenine when absorbed through the intestinal wall is not attacked by the amidases, and when acted upon by the tissue oxidases the NH_2 group in the 6 position remains, while the oxygen enters the 2 and 8 positions of the purin ring as in the formation of uric acid.

DESTRUCTION OF URIC ACID

After the uric acid has once been formed, however, it has yet to be disposed of, and the manner of its disposal has been the subject of innumerable investigations and disputes, since this is a matter of great clinical interest in connection with gout. It is in this field particularly that light has recently been thrown, with results that are both interesting and important. These results indicate that *no organism below the mammals* as yet investigated has the power to destroy uric acid, although many of them, such as birds and reptiles, produce it in great amounts and are obliged to excrete it unchanged, insoluble as it is. *All mammals* that have been studied, however, *with the important exception of man*, are able to destroy uric acid rapidly and in considerable quantities. This destruction is also an oxidation, accomplished by a specific enzyme which is appropriately called *uricase*, and the reaction seems to consist of a removal of one of the carbon atoms from the uric acid, thus converting it into the more soluble allantoin, which is then excreted as such. This reaction may be expressed by the following equation:



The change occurring in the molecule may be seen by comparing the structural formula of allantoin with that of uric acid:



The uricolytic power of different tissues varies greatly in different species and in different organs of the same species. As a rule, it is found only in the kidney and liver, other tissues showing little or no power of destroying uric acid,¹⁰ as can be seen by the table of distribution of purin enzymes given below. The uricolytic activity of tissues may be determined directly, by estimating, by quantitative methods, the destruction of uric acid added to organic extracts well supplied with oxygen, or indirectly, according to Battelli and Stern,¹⁰ by measuring the CO_2 given off by tissue extracts after addition of uric acid to them. The results by both methods seem to be in fairly close agreement.

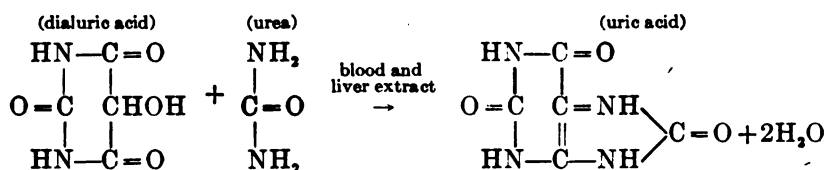
According to Wiechowski and Wiener⁵ uricase is not present in tissue plasma, but is liberated from the cells only upon their disintegration, and acts best in a slightly acid medium. It seems not to be inhibited by blood serum, as are so many other intracellular enzymes,^{5 15} but is inhibited to greater or less degree by other constituents of the tissues present in organ extracts, so that some tissues oxidize much better after being exposed to alcohol or even after some autolysis (Battelli and Stern,¹⁰) and uricase may be destroyed by the extracts of organs which do not themselves contain it (Künzel and Schittenhelm²⁸). Uricase can utilize for the oxidation of uric acid molecular oxygen such as is contained in hæmoglobin or in watery solutions, but cannot utilize active oxygen liberated by peroxides.¹⁰ By proper procedures the enzyme can be obtained with very little contaminating protein.⁵

SYNTHESIS OF URIC ACID

One of the most interesting features of uricolysis exhibited by organ extracts is the apparent reversibility of the reaction, as was first shown only a few months ago by Ascoli and Izar.²⁹ If an extract of bovine liver is allowed to act upon uric acid in the presence of an abundant supply of oxygen until the uric acid has been all or nearly all destroyed, it will again re-synthesize the uric acid if the supply of oxygen is cut off. Likewise, if arterial blood containing uric acid is perfused through a dog's liver the uric acid is destroyed, but reappears if the same blood is saturated with CO_2 and again run through the liver.⁴⁰ This re-synthesis is distinctly a ferment reaction, as boiling the liver extract destroys its

synthetic power, but the liver extract without the presence of more or less blood is devoid of synthetic action, and Preti's experiments²¹ indicate that the synthesizing enzyme is contained in the blood but not in the liver. That is, liver tissue destroys uric acid but cannot synthesize it from the cleavage products, while blood, which has little or no uricolytic power, can build it up from these fragments if in the presence of liver extract. Blood alone is unable to regenerate the destroyed uric acid, but in the presence of liver extract, even when the liver extract has been boiled, it is active in this respect. From this it is evident that the regeneration of uric acid in the absence of oxygen, after its destruction in the presence of oxygen, is not a true reversible reaction such as that of lipase and maltase. Other evidence to the same effect is afforded by the extracts of bovine kidney, which destroy uric acid actively but are not able to regenerate it on shutting off the oxygen, for if the reaction were a simple reversible one it should occur equally well with kidney and liver extract.

Ascoli and Izar have also tried the synthesis of uric acid from the various products of uric acid disintegration that are obtained by different methods of destruction.²⁰ Since allantoin and CO_2 are known to be produced by the action of uricase on uric acid, if the reaction were a reversible one the liver extract should be able to synthesize uric acid from these two substances. Such, however, is not the case, for of all the combinations tried, successful synthesis was obtained only when the liver extract acted upon *dialuric acid* and *urea*, the nature of the synthesis being shown by the following equation:



This reaction is essentially one of dehydration, while the formation of allantoin from uric acid is an oxidation, hence one reaction obviously cannot be a reversion of the other, and we must suspect the existence of two different enzymes with separate and distinct properties.

These experiments seem to settle affirmatively the old question as to whether mammalian tissues have any power of synthesis of uric acid. As far as we have yet learned, however, their synthetic power differs essentially from that of the birds and reptiles, since the latter can synthesize uric acid from simple compounds derived from non-purin sources, whereas, in the mammal only certain definite products of uricolysis can be reunited to form urea. Nevertheless, the growing mammal certainly synthesizes purins, for it builds up its tissues from milk, which is practically devoid of purine, and it has been found possible experimentally to keep animals alive on a purin-free diet while they continue to excrete purins or their products in the urine (McCollum⁸¹). In this way, at least, mammals can synthesize uric acid, by synthesizing first the tissue purins and from these forming uric acid, but how much uric acid is formed in this way under ordinary conditions of diet is quite unknown. It may be that all of the endogenous purin is of synthetic origin, and that none of the tissue purin comes from the purins of the food.

DISTRIBUTION OF PURIN ENZYMES

The striking irregularity of distribution of these enzymes of purin metabolism is quite unique in our knowledge of cellular enzymes, and must be of considerable significance in the course of both normal and pathological metabolism, hence it is worth while to consider this fact somewhat fully.

To recapitulate from the literature of the subject, the distribution of purin enzymes, according to the best existing evidence, is as follows:

Nuclease.—Present in all cells as yet investigated.

Adenase.—Present in all tissues and cells (including bacteria⁴) as yet investigated, except the following: the human foetus of three months,¹⁶ yeast cells,² rabbit's liver,^{11*} the tissues of the fetal dog up to the time of birth,¹⁷ and the lung of the human foetus,¹⁸ and it is but poorly developed in the liver of the adult dog.¹¹ According to Miller and Jones³⁹ adenase is absent (questioned⁴⁸) from human spleen, liver, pancreas, kidney, and lung.

* Schittenhelm and Schmidt do not agree with this statement, finding that rabbit liver does contain adenase, but their results seem questionable.

Guanase.—Present in all tissues and cells yet investigated except the spleen and liver of the pig,^{11 19} the pancreas of the dog,¹¹ and the human spleen.³⁹

Xanthine-oxidase.—Present in the spleen of the dog,¹¹ bovine,^{11 4 6} and horse¹²; absent from the spleen of man^{1 12 39} and pig.¹² Present in the liver of bovine,¹ rabbit,^{11 13} swine,¹¹ and man,^{1 16 39} possibly absent in liver of the dog.⁴⁸ Also found in the bovine muscle,¹⁴ intestine,⁶ lung,^{6 14} dog's lung and intestine⁴⁸ but not in the bovine thymus¹⁴ and blood,¹⁴ nor in the lung¹² and pancreas¹¹ of swine, the pancreas of the dog,¹¹ the human placenta¹⁶ nor the blood of man⁹ and sheep.⁹ It seems to be lacking in all the chief human tissues except the liver,³⁹—and the same is true of the monkey.⁴⁷ It is also missing in the yeast² and bacterial⁴ cells, and the tissues of a mollusk (*Sycotypus canaliculatus*²¹).

Uricase.—If we limit the use of this term, as recommended by Battelli and Stern¹⁰ to the oxidizing enzyme which produces allantoin and CO₂ from uric acid, and appreciate that there may possibly exist other enzymes which destroy uric acid in some other way, we find that either the kidney or liver of every mammal investigated, except man^{1 20 10 15 39} possesses uricase, while it is entirely or practically missing from every other mammalian tissue,¹⁰ and this is absent from all the tissues of birds, (goose¹⁰) and reptiles (turtle¹⁵).

Taking the most reliable investigations to be found in the literature, we find the demonstrated presence or absence of uricolytic property to be as follows:

Liver.—Present in bovine,^{6 10} dog,^{5 10 15} pig,¹⁹ rabbit,^{13 10} guinea-pig,¹⁵ sheep,¹⁰ cat,¹⁰ horse,^{7 10} dog-fish,⁴⁹ monkey;⁴⁷ absent in man,^{1 20 15 10 39} turtle,¹⁵ goose,^{10 32} and mollusk.²¹

Kidney.—Present in bovine,^{5 6 10} dog (slight),¹⁰ horse,^{8 10} rabbit;¹³ absent from the kidney of man,^{15 10 39} sheep,¹⁰ and monkey.⁴⁷

Muscles.—Present in bovine,^{6 14} and in the horse (slight);¹⁰ absent in the muscles of sheep, dog and bovine.¹⁰

Uricolysis has been found wanting in the spleen of beef,^{6 10} dog,^{8 10} pig,^{8 11} monkey,⁴⁷ sheep;¹⁰ but feebly present in the spleen of the horse;¹⁰ it is also lacking in the lung of bovine,⁶ horse,¹⁰ dog,¹⁰ monkey,⁴⁷ and sheep,¹⁰ the bovine intestine,⁶ and the blood

of man,⁹ bovine,¹⁰ dog,^{10*} sheep,^{9 10} horse,¹⁰ the pancreas of the horse,^{7 10} the brain of the horse⁷ and dog,¹⁰ and the leucocytes and bone-marrow of the dog.¹⁵

Measuring the amount of activity of uricase by the amount of CO₂ produced from uric acid by the action of tissues, the relative uricase content of different tissues in decreasing order is, according to Battelli and Stern,¹⁰ as follows: Beef kidney, horse liver, cat liver, dog liver, rabbit liver, horse kidney, and sheep liver; beef liver and dog kidney have only slight uricolytic power, and the other tissues have no distinct activity. The fresh tissues seem to contain inhibiting substances which can be removed by alcohol, and the relative activity of such alcohol-treated tissues is not in quite the same order as that given above.

An important fact brought out by Künzel and Schittenhelm²⁸ is that the enzymes of one organ may influence the activity of the enzymes in another organ. For example, bovine spleen extract rapidly converts xanthine into uric acid but does not destroy uric acid, whereas the kidney extract is actively uricolytic; but if extracts of the two organs are mixed, both the uric acid formation and destruction are markedly inhibited. Control experiments showed that this was due to thermolabile constituents of the organs, presumably enzymes. This observation indicates that conditions in the entire body, when one organ may exert an influence upon another, are perhaps quite different from experimental conditions, and so *the application of experimental results to physiological and pathological problems must be guarded*. For example, although the bovine spleen shows no evidence of uricolytic power *in vitro*, yet it is possible that the spleen possesses uricolytic enzymes which can act while the organ is in the living body, but which are inhibited *in vitro* by the more active uric-acid-forming enzyme.

Another point which should be mentioned is the rapidity with which the several purin enzymes act. For example, if bovine spleen acts upon guanine in the presence of air for but 10 or 15 minutes the guanine will have all disappeared by that time, being replaced by xanthine and uric acid, and in an hour the complete conversion of the xanthine to uric acid may have been accomplished²⁸; 350 c.c. watery extract of bovine kidney will entirely

* Preti²² states that dog's blood is actively uricolytic.

destroy 0.3 Gm. uric acid in from four to seven hours,¹⁶ and one gramme of dried powdered bovine kidney will destroy 0.12 Gm. uric acid in four hours.⁵ On the whole the deamidizing enzymes act more rapidly,⁴ and are more resistant to autolytic disintegration than are the oxidizing enzymes. In the living organism also the reactions seem to take place with corresponding rapidity, for Bloch³⁸ found that three hours after the taking of nucleic acid into the stomach a large quantity of uric acid appeared in the blood.

One of the most interesting of the observations upon the purin enzymes concerns their *development during the growth* of the mammalian foetus, for the several enzymes appear one at a time and the entire equipment is not obtained much before birth. Mendel and Mitchell²² found that in the embryo pig the nuclease is present in the earliest stages, and that the adenase appears at least by the time the length of the foetus has reached 50 mm., but that the xanthine-oxidase is present soon after birth, while the uricolytic enzyme does not appear until later. Jones and Austrian²⁶ could find no evidence of adenase in embryo pigs' livers until the embryos had reached a length of 150 to 170 cm., but otherwise their results are in harmony with Mendel and Mitchell. Study of the human foetus in my own laboratory has shown a strikingly similar course of development. At three months only guanase seems to be present, adenine not being destroyed at this stage, although at the fifth month the foetus destroys adenine vigorously. The xanthin-oxidase, however, is found only at or near full term, and then chiefly in the liver, although perhaps present in slight amounts in other tissues. The human foetus, like the adult human, at no time possesses active uricolytic power, while the human placenta seems not to contain either uricase or xanthine-oxidase, although provided with guanase and adenase.

This sequence of development when compared with the distribution of purin enzymes in the animal kingdom, suggests that chemically as well as morphologically the individual in its development reflects the development of the species to which it belongs. Thus in a unicellular organism, the yeast, there are found only nuclease and guanase, so that the human foetus at three months is equipped with the same enzymes as the yeast cell. At the fifth

month, when it has acquired adenase but not xanthine-oxidase, the human foetus may be compared with the mollusk which also lacks xanthine-oxidase but possesses the nuclease and the two amidases. At birth the human and pig foetus are probably in the same condition as to purin enzymes as the reptile and the bird, being able to form uric acid but not to destroy it. *The uricase seems to be a late development, which is acquired only by the mammals—by all of them except man.*

THE BEARING OF THE OBSERVATIONS ON PURIN ENZYMES UPON THE
PATHOGENESIS OF GOUT

The statement that man alone of all the mammals is unable to destroy uric acid, is one that must necessarily challenge opposition. In the first place it seems, *a priori*, improbable that so highly developed an organism as man should be in this respect less developed than all the other mammals; and secondly, there has existed experimental evidence which has been accepted for a long time as proving that the human body does destroy uric acid. Our conception of gout must be dependent upon our understanding of the normal metabolism of purins, especially the power of the normal body to destroy uric acid, hence it is essential to establish positively whether such destruction of uric acid does or does not take place in man, and the evidence upon which we have based the idea that it does not take place is entitled to critical consideration. This evidence has not only been obtained by experiments performed both *in vitro* and *in vivo*, but it is supported by many facts concerning human metabolism which have long been recognized and accepted.

The experiments *in vitro* consist in permitting extracts of various animal tissues to act upon solutions of uric acid in the presence of an abundant supply of oxygen at body temperature; and in some instances the enzymes have been first freed from most of the associated tissue elements.⁵ It is agreed by all those who have most recently performed such experiments (Künzel and Schittenhelm,¹ Wiechowski,²⁰ Wells and Corper,¹⁵ Miller and Jones,³⁹) that under the same conditions in which the liver or kidney of other mammals will quantitatively destroy considerable amounts of uric acid, the human tissues will not destroy any appreciable

quantity of it. If, for example, we make an emulsion or extract of 50 Gms. of dog liver in 300 c.c. of water, and a similar preparation of human liver, and permit them to act side by side under identical conditions upon 0.2 Gm. of uric acid at 40° C. in the presence of an active air current, at the end of 6 to 12 hours it will be found that there is not a trace of free purin present in the dog-liver extract, while even after 48 hours or more the uric acid added to the human liver can be recovered with no loss whatever, beyond such loss as is inseparable from the analytical methods. Indeed, if enough human liver is used to yield appreciable amounts of free purins through autolysis we may find more uric acid after 48 hours than in the beginning, since the xanthine-oxidase of the liver will form uric acid from the free purins. That is, human liver will form uric acid from its own purins under the same conditions as permit dog liver to destroy not only its own purins, but also large amounts of uric acid added to it.

Another method of experimentation, devised by Battelli and Stern,¹⁰ consists in measuring the amount of CO₂ given off in the oxidation of uric acid to allantoin by the tissue extracts when uric acid is added to them. Their results corroborate completely those obtained by the other, more direct, method, as they found that no human tissues or organs gave evidence of the presence of uricase, while with every other mammal either the liver or the kidney or both were actively uricolytic. The harmony of the results obtained by such totally different methods is the best evidence of their reliability.

If, however, we had only this evidence which has been obtained with dead tissues *in vitro*, we should not be warranted in transferring the results without qualification to the elucidation of processes which take place within the living body, no matter how consistent and reliable the results of the experiments might be. But we find that studies of metabolism in living animals under both normal and experimental conditions are entirely in agreement with the thesis that the human organism differs from the other mammals in its inability to destroy uric acid.

In the first place we have the recognized peculiarity of man in excreting considerable amounts of uric acid daily, even when upon a diet free from purins, and the marked rise in uric acid

excretion when purin-rich food is taken. All other mammals whose urine has been investigated excrete relatively small amounts of uric acid, its place apparently being taken by allantoin (Wiechowski^{20 41 42}). As mentioned previously, the result of the action of uricase upon uric acid *in vitro* is the production of allantoin, and evidently the same product is obtained when uric acid is destroyed in the living organism. Thus, if we give a purin-rich diet or inject uric acid subcutaneously into mammals, there is only a slight rise in the uric acid excreted and a large rise in the allantoin, corresponding to the amount of purin or uric acid destroyed. Under the same conditions the human organism excretes increased amounts of uric acid, and no appreciable amounts of allantoin. The careful studies of Wiechowski, to whom we owe most of our best information on this point, show that the human urine never contains more than the most insignificant traces of allantoin, recognizable only with great difficulty,⁴² in contrast to the urine of other mammals which excrete little uric acid and much allantoin. As his experiments have also shown that neither man nor other animals can destroy allantoin which has been subcutaneously injected, but eliminate it unchanged in the urine, the only conclusion that can be drawn is that the human organism differs from all the other mammals in having little or no power to oxidize uric acid into allantoin, thus showing that the results obtained with organ extracts correctly represent the metabolic activity of the same organs in the living.

One objection that may be raised is that possibly the human tissues destroy uric acid by some other process than oxidation into allantoin. In favor of this might be quoted the well-known fact that of the purins taken in the food by man but 50 to 60 per cent. appears in the urine as uric acid; hence it may be assumed that the other 40 to 50 per cent. is destroyed without producing allantoin. Against this assumption may be advanced the following arguments: First, it is less probable that one mammal should have a peculiar method of destroying uric acid, unknown in any other mammal, than that it should fail to develop a special enzyme which embryological and comparative investigations show is the last of the entire series to appear; and the demonstration of Wiechowski that normally the human urine contains a few (7-14)

milligrammes of allantoin per day seems to establish that what little power of uricolysis is possessed by man is accomplished in the same way as in other mammals. Man is defective quantitatively, not qualitatively, in his power to oxidize uric acid into allantoin. Second, the failure of half the purin taken in the food to appear in the urine as uric acid is not evidence of uric acid destruction, because the purins are probably not all absorbed and because bacterial destruction in the intestine is probable. Third, experiments made by Wiechowski and others indicate that when uric acid is injected subcutaneously in man, from 60 to 90 per cent. of it is excreted in the urine within 24 to 48 hours, which is probably as much as can be absorbed in this time. Fourth, in chronic nephritis, when the power of the kidneys to eliminate uric acid is impaired, we find that the retained uric acid is not destroyed but is deposited in the joint cartilages and in the viscera just as it is in true gout.⁴⁴ Fifth, in diseases associated with high nuclear catabolism, such as leukæmia and pneumonia, the uric acid which is formed from the nuclear purins is excreted in large amounts, and there is no evidence of its being destroyed.

The metabolic peculiarity of man which renders him unable to oxidize uric acid into the more soluble and less irritating allantoin, is undoubtedly the reason for his susceptibility to gout with uric acid deposition in his joints and tissues. Comparative pathology affords conclusive support of this view, for while no other mammal is known to have gout with uric acid retention and deposition, yet this condition is met with often in birds, and is readily produced experimentally in fowls, which share with man the lack of uricolytic enzymes. And furthermore, the occurrence of a form of gout in swine, the so-called *guanine gout*, which is characterized by the deposition of guanine rather than uric acid,⁴⁵ is in striking harmony with the fact that the liver of swine is peculiar in its lack of guanase, and consequently cannot destroy guanine, although it destroys uric acid vigorously.

We must, therefore, conclude that *because man cannot destroy uric acid he is always a potential victim of uric acid retention and deposition*. That the uric acid retention is the cause of the manifestations of gout is not here asserted, for there is abundant evidence to the contrary. But retained uric acid is not harmless,

as is well shown by the toxic effects observed by Wiechowski when he injected uric acid subcutaneously into himself, and furthermore, if it is retained and accumulates in the tissue fluids it must, by the law of mass action, interfere with the several chemical processes which lead up to its formation, thus causing an excess of the other purins and their antecedents also to be present in the tissue fluids. Whether the intoxication from these sources accounts for all the features of gout or not it is not our purpose to discuss, although feeling strongly that the ultimate decision will probably be in the negative, in view of the well established absence of true gout in spite of long standing uric acid retention and accumulation in chronic nephritis and chronic leukæmia. What we feel has been established by our recent accretions of knowledge in this field, is the following: All hypotheses which assume that gout is due to a loss or reduction of normal power to destroy uric acid must be discarded, since the human body has little or no such power under normal conditions. By elimination of these hypotheses support is gained for the view that defective elimination of normal amounts of uric acid is the fundamental fault which is responsible for the established metabolic abnormalities of gout, namely, that the blood of the gouty contains at all times abnormally large quantities of uric acid, and that ingested purins are eliminated less rapidly and completely by the gouty than by normal individuals (Brugsch and Schittenhelm⁴³). Also, by demonstrating that man differs from all other mammals in being unable to destroy the uric acid he forms, we have a satisfactory explanation of why he alone of all the mammals frequently suffers from deposition of uric acid in his joints and tissues. How much of the symptomatology and pathology of gout is to be attributed to uric acid, how much to other purins, and how much to unknown factors, the experiments discussed above do not attempt to elucidate; nor do they explain whether the retention of uric acid is a cause or a result of the gout, or whether this retention is due to a loss by the renal epithelium of the power to excrete uric acid or to some change in the conditions of solution of the uric acid in the circulating blood whereby it cannot be taken out of the blood by the kidneys. These problems, however, are in a much better position for solution now that we have secured a better understand-

ing of the processes and forces by which purin metabolism is accomplished and are better able to follow out the steps of purin metabolism in health and in disease.

BIBLIOGRAPHY

1. KÜNZEL and SCHITTENHELM: *Zentralbl. f. Path. u. Phys. Stoffwech.*, 1908, iii, 721.
2. STRAUGHN and JONES: *Jour. Biol. Chem.*, 1909, vi.
3. SCHITTENHELM: *Ztschr. physiol. Chem.*, 1905, xlvi, 354.
4. SCHITTENHELM: *Ztschr. physiol. Chem.*, 1908, lvii, 21.
5. WIECHOWSKI and WIENER: *Hofmeister's Beitr.*, 1907, ix, 247.
6. KÜNZEL and SCHITTENHELM: *Ztschr. exp. Path. u. Ther.*, 1908, v, 389.
7. ALMAGIA: *Hofmeister's Beitr.*, 1905, vii, 459.
8. BRUGSCH and SCHITTENHELM: *Ztschr. exp. Path. u. Ther.*, 1908, v, 406.
9. BRUGSCH and SCHITTENHELM: *Ztschr. exp. Path. u. Ther.*, 1907, iv, 446.
10. BATTELLI and STERN: *Biochem. Ztschr.*, 1909, xix, 219.
11. JONES and AUSTRIAN: *Ztschr. physiol. Chem.*, 1906, xlviii, 110.
12. SCHITTENHELM: *Ztschr. physiol. Chem.*, 1905, xlvi, 354.
13. SCHITTENHELM and SCHMIDT: *Ibid.*, 1907, l, 30.
14. WIENER: *Arch. exp. Path. u. Pharm.*, 1899, xlii, 375.
15. WELLS and CORPER: *Jour. Biol. Chem.*, 1909, vi, 321.
16. WELLS and CORPER: *Ibid.*, 1909, vi, 469.
17. JONES and DE ÁNGULO: *Proc. Amer. Soc. Biol. Chem.*, 1909, i, 193.
18. SCHITTENHELM and SCHMIDT: *Ztschr. exp. Path. u. Ther.*, 1907, iv, 428.
19. MENDEL and MITCHELL: *Amer. Jour. Physiol.*, 1907, xx, 97.
20. WIECHOWSKI: *Arch. exp. Path. u. Pharm.*, 1909, lx, 185.
21. PRETI: *Ztschr. physiol. Chem.*, 1909, lxii, 354.
22. MENDEL and WELLS: *Amer. Jour. Physiol.*, 1909, xxiv, 170.
23. WELLS: *Jour. Med. Research*, 1908, x, 149.
24. SACHS: *Ztschr. physiol. Chem.*, 1905, xlvi, 337.
25. JONES: *Jour. Biol. Chem.*, 1908, v, 1.
26. JONES and AUSTRIAN: *Jour. Biol. Chem.*, 1907, iii, 227.
27. BURIAN: *Ztschr. physiol. Chem.*, 1904, xliii, 497.
28. KÜNZEL and SCHITTENHELM: *Ztschr. exp. Path. u. Ther.*, 1908, v, 393.
29. ASCOLI and IZAR: *Ztschr. physiol. Chem.*, 1909, lviii, 529.
30. ASCOLI and IZAR: *Ibid.*, 1909, lxii, 347.
31. MCCOLLUM: *Amer. Jour. Physiol.*, 1909, xxv, 120.
32. FRIEDMANN and MANDEL: *Arch. f. exp. Path. u. Pharm.*, Suppl., 1908, p. 199.
33. ABDERHALDEN and SCHITTENHELM: *Ztschr. physiol. Chem.*, 1906, xlvii, 452.
34. FOA: *Archivo di Fisiologia*, 1907, iv, 98.
35. JONES and WINTERNITZ: *Ztschr. physiol. Chem.*, 1905, xlv, 1.
36. MINKOWSKI: *Arch. exp. Path. u. Pharm.*, 1898, xli, 375.
37. NICOLAÏER: *Ztschr. klin. Med.*, 1902, xlv, 359.
38. BLOCH: *Deut. Arch. f. klin. Med.*, 1905, lxxxiii, 500.
39. MILLER and JONES: *Ztschr. physiol. Chem.*, 1909, lxi, 394.
40. BEZZOLA, IZAR, and PRETI: *Ztschr. physiol. Chem.*, 1909, lxii, 229.
41. WIECHOWSKI: *Hofmeister's Beitr.*, 1907, xi, 109.
42. WIECHOWSKI: *Biochem. Ztschr.*, 1909, xix, 368.
43. BRUGSCH and SCHITTENHELM: *Ztschr. f. exp. Path. u. Ther.*, 1907, iv, 550.
44. *Ibid.*, p. 532.
45. BRUGSCH: *Ibid.*, 1909, vi, 278.
46. SCHITTENHELM and BENDIX: *Ztschr. physiol. Chem.*, 1906, xlviii, 140.
47. WELLS: *Jour. Biol. Chem.*, 1910, vii, 171.
48. SCHITTENHELM: *Zentralbl. f. Path. u. Phys. Stoffwech.*, 1909, iv, 801.
49. SCAFFIDI: *Biochem. Zeitschr.*, 1909, xviii, 506.

CHRONIC MUCOUS COLITIS

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THIS paper is a résumé of one hundred and fifty-eight cases of chronic mucous colitis. Only those cases were included in this series in which the affection, from the clinical standpoint, was limited to the colon. This excluded the catarrhal conditions of the large bowel that were associated with marked disturbances of the stomach and small intestine, as evidenced clinically by the presence of undigested food in the bowel movements.

In the cases that furnish the basis of this paper, the stools were studied macroscopically in all, microscopically and chemically in a considerable number, and bacteriologically in six. The limited number of the last two groups do not permit conclusions to be formed from them. The subject, therefore, is considered purely from the clinical side. Only old cases were included in this series whose after-history is known. Of the hundred and fifty-eight cases, sixty-seven were males and ninety-one females. The youngest was a boy of six; the oldest, a woman of sixty-five—75 per cent. of the patients were from twenty to fifty years of age. The disease had existed from a few months to twenty or more years. One hundred and forty-two, or 90 per cent., had disturbances in nutrition, as evidenced by loss of weight varying from eight or ten to forty pounds below weight in health. The greater curvature of the stomach was lower than normal in one hundred and eighteen of the cases. The right kidney was palpable in fifty-three; both kidneys in fifteen and the left alone in two cases. Ninety-two had the "habitus enteroptoticus," i.e., a long, narrow thorax with sharp costal angle. Since this predisposes to general enteroptosis, there being in such a condition greater longitudinal than transverse room for the abdominal viscera, it is a question in our mind whether this anatomical condition does

not predispose to the development of colitis, as will be indicated below.

One hundred and fifty-four of the one hundred and fifty-eight patients were constipated, and had been so from several months to twenty years before they applied for treatment. Of the one hundred and fifty-four who had chronic constipation, the constipation was of the spastic type in one hundred and thirty-one.

We believe colitis to be a superficial inflammation of the large bowel secondary to chronic constipation, and that from the practical standpoint, colitis and chronic spastic constipation should be considered the same.

Atonic constipation is void of abdominal symptoms, with the exception of constipation itself. Spastic constipation is accompanied by a chain of symptoms that should prevent confusion in differentiating one variety of chronic constipation from the other. In spastic constipation, the stool is of small calibre; the rectum is empty to the palpating finger; laxatives and enemata are unsatisfactory; the patient suffers from chronic flatulence and its reflex, cardiac, gastric and nervous symptoms, and there occurs the passage of mucus proportionate to the duration of the disease and the irritation of the mucous glands by stagnation of the faeces in the colon.

The evolution of chronic constipation is about as follows: The atonic is the first stage. It may persist for years or decades before the second or spastic stage. As a result of long-continued stagnation of intestinal contents in the atonic period, the colon becomes irritable and hypertonic and a spasm of its musculature results as an additional factor to the causes that exist in atonic constipation. The abnormal amount of mucus secreted, because of the constant irritation of the mucous glands, undergoes fermentation and greatly increases the amount of gas in the large intestine. The gas and mucus of spastic constipation are responsible and account for the abdominal distress not present in the atonic stage of the disease.

In this series, the length of time that atonic constipation had existed before passing into the spastic stage seemed to depend largely upon the nervous organization of the patient. In those of stable nervous organization, the constipation did not become spastic for years or decades, while in the nervous types, the spastic stage,

in a few instances, developed after atonic constipation had existed for only a few months.

We have dealt at considerable length with this phase of the subject because it is our belief that chronic constipation is the cause, that in it is to be found the pathogenesis of the disease known as chronic mucous colitis, and that it is the indication for its treatment.

One of the most common diagnoses that had previously been made in this series was "neurasthenia" and treatment had been directed to the nervous condition of the patient. A large number had been treated for stomach trouble, others for nervous heart, etc. There should be no great difficulty in differentiating the nervous, gastric, cardiac and other reflex symptoms secondary to colitis from those of organic lesions of these organs, if it is kept in mind that in colitis the symptoms are greatly ameliorated when the bowels are kept freely open by laxatives and absent when the constipation is cured.

The abdominal distress in these cases seemed directly dependent upon and proportionate to the amount of mucus and gas in the large bowel. Mucous colic and the so-called "wind colic" represented the extremes of pain; graduated up to these were all degrees of sensory discomforts,—distention, uneasiness, distress and actual pain. Typically, the pain of colitis is left-sided, in the region of the sigmoid. In this series, patients as frequently complained of general abdominal distress, and in some cases the abdominal pain and discomfort was most marked in the right colon. When this was the case, and also in many instances when the transverse portion of the colon was most involved, considerable difficulty was encountered, and prolonged observation was required to differentiate the suspected colitis from indefinite and atypical gall-bladder disease, chronic appendicitis, chronic peptic ulcer, and other surgical affections. But in the majority of cases it was not difficult to establish the fact that the symptoms in colitis were controlled by keeping the bowels freely open. This was the crucial differential diagnostic point, for in no other chronic disease of the abdomen are the symptoms so closely dependent upon the condition of the bowels.

In twelve cases of this group, there was, in addition to typical mucous colitis, chronic disease of the gall-bladder, nine without and three with gall-stones, all of which were surgically treated. Eleven had chronic appendicitis and were operated upon. Two had what was clinically diagnosed as acute duodenal ulcer and seven as acute gastric ulcer; the symptoms of both disappeared under prolonged medical treatment. Two of the latter have since recurred and should be treated surgically. Chronic ulcer of the stomach was present in three cases, all of which were treated surgically. Six others had received surgical treatment before coming under observation; of these, two were for chronic appendicitis, one for chronic cholecystitis and three for "dilation" of the stomach.

In none of the cases treated surgically for gall-bladder and stomach disease, did operation have any favorable influence upon the colitis. In three of the thirteen that were operated upon for chronic appendicitis, the colitis was permanently cured. In the remaining ten cases, operation had no permanent effect upon the colitis.

The treatment was based upon the principle that chronic mucous colitis is secondary to chronic constipation. The indication for treatment was, therefore, the cure of the latter. In our opinion the difficulties encountered in the cure of chronic constipation and the lack of our knowledge of its pathogenesis are responsible for the difficulty in curing mucous colitis. Contrary to usual custom, no treatment was directed primarily to the nervous condition of the patient. The so-called neurasthenia and nervousness from which most of these cases had previously been told they had been suffering disappeared of themselves when the spastic constipation was cured.

Endeavor was made to restore the abdominal and pelvic organs to their normal anatomical relations, when indicated, by properly fitting abdominal supports or corsets and by operations upon the uterus when it was displaced with adhesions. In one case the right kidney was surgically anchored; in two cases, colonic adhesions were without doubt the immediate cause of constipation and the resulting colitis. One of these cases was permanently cured by surgical treatment. In the other, re-formation of adhesions occurred two months after operation, as shown at autopsy.

Instead of discussing under separate heads the various symp-

tomatic indications, we shall outline the treatment adopted in this series. Before doing so, it should be emphasized that the average colitis patient, besides suffering from spastic constipation, is sub-nourished and has abdominal distress caused by the presence of gas and mucus in the colon that in turn produce many reflex symptoms,—palpitation of the heart, dyspepsia, nervous irritability, mental depression, insomnia and other nervous manifestations.

Most of the cases were put in bed and given a combination of the rest treatment and measures directed to the relief of constipation. The more severe cases were, whenever possible, given institutional care where the details of treatment could be closely supervised and where they could have complete rest from home and business cares.

The diet in most instances consisted of raw eggs and milk, because it is sufficiently nutritious and furnishes small intestinal residue, and is therefore non-irritating. We have not had good results with the coarse diet recommended by Noorden. Such a diet is suitable for atonic constipation, but not for the spastic stage when the musculature of the colon is hypertonic and irritable. Following the relaxation of the colon, as evidenced by larger calibre stool, absence of flatulence and abdominal distress, a coarse diet that both mechanically and chemically stimulates peristalsis, as indicated in atonic constipation, was substituted. It is this latter form of diet in conjunction with other measures that colitis patients must religiously follow to prevent a recurrence of their trouble.

The details of diet in this series were about as follows, variations being made as per indications in individual cases: Six feedings were given daily at three-hour intervals, from 6.30 A.M. to 9.30 P.M., an egg-feeding alternating with a milk-feeding. Patients tired less quickly of the diet when fed by this method than when the eggs and milk were served together. The success in the forced feeding depended upon ascending doses of nourishment. The first day, one raw egg (with lemon juice, sherry or salt and pepper) and one glass of milk (with or without lime water) were given alternately every three hours. Each succeeding day, one egg and one glass of milk were added until from four to six eggs

and two and one-half to three glasses of milk were given alternately at the respective feedings. We rarely found patients unable to follow out this diet scheme.

Improvement in nutrition is very important in the treatment of chronic colitis, because it is the most effective weapon for reducing the high irritability of the nervous system, as evidenced by the well-known beneficial results of rest and "forced feeding" in neurasthenic conditions.

When hyperacidity of the gastric juice was associated with chronic colitis, a glass of Carlsbad water or a dram of its salts to a glass of warm water was given an hour before the first feeding. In subacidity of the stomach, Kissingen or some other sodium chloride water was used instead. In rare cases when diarrhoea instead of constipation was present, the mineral waters as above indicated were served hot.

To favor the relaxation of the colonic spasm, belladonna or atropine (usually the tincture of the former in ten-drop doses), was given three or four times daily. When indicated, various carminatives and nerve sedatives were added for the relief of flatulence or troublesome nervous symptoms at the beginning of the treatment.

For the relief of abdominal distress, hot fomentations to the abdomen were used three or four times a day and a Priessnitz Compress worn at night (a linen towel wrung out of cold water, wrapped snugly around the abdomen and covered with four or five layers of dry flannel).

Depending upon the amount of mucus and gas, as clinically evidenced by abdominal distress and flatulence, the colon was flushed once or twice daily. No effort was made to introduce the colon tube more than six or eight inches. Warm, normal saline solution was the usual irrigation fluid used, the quantity being one or two quarts. In some few instances, plain water was less irritating and painful. Often carminative teas caused less abdominal discomfort than either of the above. Warm olive oil or linseed oil, as much as could be introduced and comfortably retained, was injected before retiring in cases with dry, hard and lumpy stools. In severe cases, it was necessary to resort to licorice powder or cascara the first week or ten days of treatment to keep the bowels

21

well open so that the patient could tolerate the non-irritating and nutritious but constipating diet of eggs and milk.

After the disappearance of signs and evidences of spastic constipation, the coarse diet indicated in atonic constipation was substituted, and all forms of exercise prescribed which tend to prevent the return of chronic constipation.

Twenty-eight of the one hundred and fifty-eight cases have been lost sight of and are therefore not included in the tabulated results. Of the one hundred and thirty cases whose after history is known, eighteen, or 14 per cent., received no benefit at all or soon relapsed after the cessation of active treatment. Thirty-six, or 28 per cent., were greatly benefited—by which is meant freedom from symptoms, except those following occasional temporary return of constipation. Seventy-six, or 58 per cent., were cured.

Surgery

THE DIAGNOSTIC VALUE AND THERAPEUTIC EFFECTS OF THE BISMUTH PASTE IN CHRONIC SUPPURATION *

BY EMIL G. BECK, M.D.

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A RÉSUMÉ of three years' experience with the use of the bismuth paste may, at this time, prove profitable not only to those who wish to employ it, but also to those who have tried it and have, for some reason, not obtained satisfactory results.

In order to present the subject most advantageously I shall bring out only the essential and most practical points, as, for instance, the causes of failures, the precaution against bismuth poisoning and the most recent advances in the diagnostic method, especially the *stereo-radiograph*.

For a detailed description of technic, experimental work and the statistical studies, I refer the reader to my previous publications.^{1 2 3 4 5 6}

The paste, which consists of one part of bismuth subnitrate and two parts of white or yellow sterile vaseline, has been applied for two principal purposes: *First*, for *diagnosis*, or rather, for *exploration of the boundaries of sinuses and abscess cavities*; *second*, for *curative purposes in chronic suppurations*.

DIAGNOSTIC METHOD

This consists of injecting, with a glass or metal syringe (Fig. 1), a quantity of bismuth paste (liquefied by heating in a water bath) into an opening of a sinus until one feels reasonably certain that all ramifications have been filled. The paste, thus injected, will rapidly congeal and remain in the sinuses long enough to permit of

* Read before the Cleveland Academy of Medicine, Jan. 19, 1910.

taking a radiograph. The radiograph thus obtained will enable us to view not only a true picture of the hidden labyrinth of channels, but will also lead us to the focus from which the disease originally started, and in many instances reveal errors in our diagnosis which may cause us to change our entire course of treatment.

It will require but little persuasion to convince even the most skeptical of the diagnostic value of this method. A glance at the radiographs in which the network of tortuous sinuses is clearly shown teaches us its advantages. We can all recall instances in which such a radiograph would have been of great assistance, and would have spared many an unfortunate a useless operation.

Formerly, we had to rely upon the probe or the colored fluids as pathfinders of sinuses, but these served as guides during the operation, while, only with this new method, are we able to make a correct anatomical diagnosis before an operation is decided upon, and thus we are able to discriminate between operable and non-operable cases.

If an operation is decided upon, then the procedure is carried out with more thoroughness and precision, as we can work with definite plans before us.

In perfecting this new diagnostic method I have found a most valuable improvement in the employment of *stereoscopic* radiographs instead of the single plates. While the single radiograph is simpler and usually quite satisfactory, it is nevertheless only a shadow picture of the object placed between the anode of the X-ray tube and the sensitive plate. The shadows thus produced by the bismuth paste injected into the sinuses all appear in one plane, making it difficult to judge their relation to the surrounding structures. We cannot discern whether the paste in a sinus runs through the bone, in front or behind it. There are still other objections to the single plate, such as the distortion of the size of the shadows, due to oblique exposures, etc. Their discussion, however, would lead us too deeply into the domain of radiography.

The stereoscopic method, which consists of the taking of two separate radiographs of the same region of the body from different viewpoints without changing the position of the parts during the exposure, practically overcomes all objections to the single plate. The focusing or fusion of the two radiographs by means of a pair

of prisms builds up a translucent body, resembling a glass model. The radiograph really ceases to be a shadow. All structures stand out in relief, the plastic effect produces clearer outline of structure, and the injected paste stands out distinctly, so that its relation to other structures is easily estimated. Moreover, the stereoscope produces a true optical view, thus correcting all distortions and magnifications of shadows.

We have found the stereoscopic method of such advantage that we have entirely lost sight of its additional cost, and now employ it whenever it is feasible, not only for diagnosis of sinuses, but practically in all cases including that of aiding the diagnosis in pulmonary tuberculosis.

It is needless to say that it requires a certain amount of practice to interpret all radiographs, but the stereoscopic method facilitates this interpretation.

The best results obtained in studying a stereo-radiograph are by examining the original large-sized plates. This requires the use of a pair of prisms which one may very quickly become familiar with (Fig. 2).

For practical purposes, and, as a matter of convenience, reductions from the original plates may be made and the pictures can then be viewed by means of the hand-stereoscope. However, some of the details are lost in the process of reduction.

As an illustration of the diagnostic advantage of stereo-radiographs I cite the following cases:

Renal Sinus.—R. P., boy, ten years old. Has a sinus in his left lumbar region, which has persisted in discharging pus for about two years following an abscess within the pelvis. The radiogram (Fig. 3) brings out the surprising fact that the sinus extends not only downward into the pelvis, but that another channel exists and extends upward into the kidney, and there the paste maps out the contour of the pelvis of the kidney. This cleared up the diagnostic puzzle as to why the sinus secreted large quantities of watery secretions (as much as 10 ounces a day), in addition to occasional discharges of pus.

Liver Abscess Following Appendicitis.—A. L., 27 years old, a robust cab driver, was suddenly attacked July 28, 1909, with an acute appendicitis. An emergency operation consisted in removing

FIG. 2.

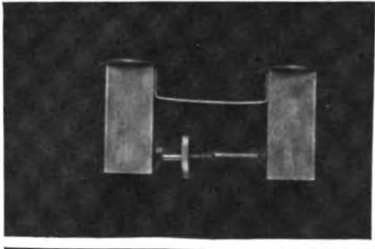


FIG. 1.

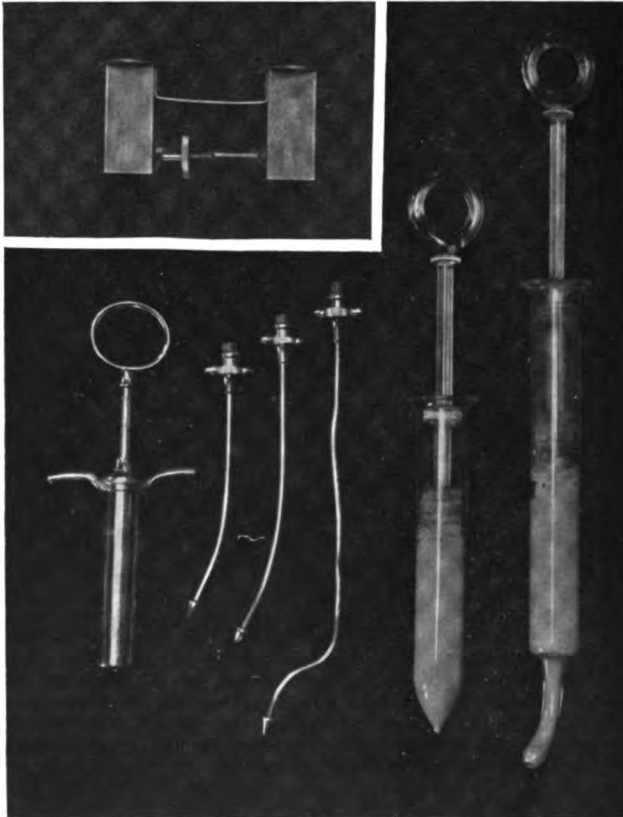
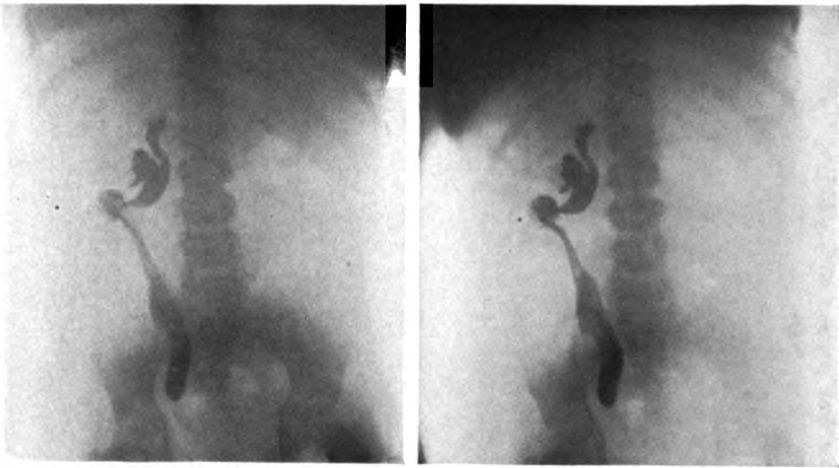


FIG. 1.—Metal and glass syringes used for bismuth paste injection.

FIG. 2.—Stereoscopic prism glasses.

FIG. 3.



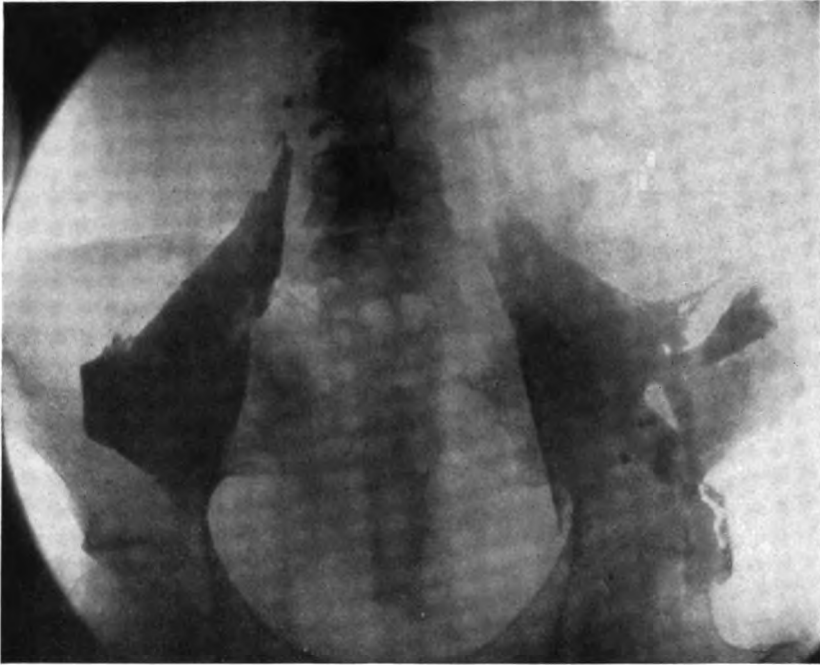
Renal sinus disclosed by paste injection. (This is a positive stereoscopic plate, and should be compared with the negative illustration, Fig. 11.) The two views have been placed less than the interpupillary distance apart so that the perspective may be obtained without a stereoscope: Hold the book 15 or 20 inches from the eyes in a good light and relax the convergence of the eyes (as if looking off to a great distance) until corresponding points of the two views overlap. After a few trials the convergence can usually be relaxed while accommodation is regained or maintained spontaneously, and a perfect stereoscopic plate obtained.

FIG. 4.



Liver abscess following appendicitis, paste showing communication.

FIG. 5.



Double psoas abscess without destruction of vertebrae.

FIG. 6.



Rectal fistula originating in pelvis—closure by bismuth after sixth operation failed.

a ruptured gangrenous appendix, diffuse peritonitis was present. With good drainage, Fowler position, and continuous "Murphy" irrigation, I succeeded in carrying him through the shock and four weeks later he left the hospital with the abdominal wound closed. However, his temperature still rose to 100° or 101° F. every day and he complained of pain in his chest. This condition became much aggravated and within a week symptoms of abscess near the liver were manifest. He developed a cough and two days later he suddenly expectorated large quantities of green, very fetid pus. At this time the abdominal wound reopened and discharged the same character of pus. An injection of the paste into the appendiceal incision proved that the original abscess of the appendix communicated with the abscess of the liver and the latter had evidently ruptured into a bronchus, since he expectorated a portion of the injected paste. A radiograph (Fig. 4), taken a few days later, demonstrated the correctness of our diagnosis. The patient was treated with injections of the bismuth paste and the lung is now entirely clear; cough has ceased and sinus is now closed. The patient has gained twenty pounds since the rupture of the abscess.

Double Psoas Abscess Without Destruction of Vertebrae.—Miss M. K., 18 years old. Was in perfect health until two years ago. September, 1907, she fell and injured the tip of her coccyx. Thereafter she was constantly ill, and in December, 1908, an abscess developed above the right Poupart's ligament. Two weeks later the abscess was lanced by the attending physician and drainage established. In January, 1909, another abscess formed on the left side, in relatively the same region, and this was also incised and drained. Both resulting sinuses persisted in discharging profusely, so much so that in order to maintain a semblance of cleanliness the dressings had to be changed two to three times daily. Radiographs of the spine failed to disclose any destruction of vertebrae, and a radiograph taken after an injection of bismuth paste furnished a remarkable picture (Fig. 5). The two abscess cavities are shown to be symmetrical, both triangular in form, having sharp borders, unlike those following psoas abscess. The diagnosis was for a time doubtful, but we have discovered that the intervertebral disc between the third and fourth lumbar vertebrae was missing, and in the absence of any other finding we concluded that in this space lay the

focus of infection. The patient is still under treatment, and while her condition is much improved, the discharge greatly diminished, and one sinus closed, the final outcome is still problematical.

The bismuth paste method of diagnosis is especially valuable in cases of rectal fistulæ. I have encountered examples in which repeated operations had failed and upon injection of the paste it was discovered that they were not rectal fistulæ at all, but sinuses resulting either from a pelvic abscess or sacral tuberculosis. The abscess happens to produce its outlet so near the anus that one is apt to mistake it for a rectal fistula and divide the sphincter, thus adding an incontinence, and simply transposing the mouth of the sinus from the outside into the interior of the rectum.

In children it happens not infrequently that spondylitis produces a sinus near the rectum. Are we to assume that every sinus near the rectum must be a rectal fistula? Certainly not. The following case illustrates the fallacy of such a supposition:

Rectal Fistula Originating in the Pelvis.—The patient, a lady, 30 years old, has since 1900 undergone six operations for rectal fistula, all of which failed to stop the profuse and irritating pus discharge. The last operation was very extensive and produced incontinence of fæces. In this condition the patient came to me in January, 1908, when I made the first bismuth paste injection. A radiogram (Fig. 6) disclosed that the fistula had its origin high up in the pelvis. Several sinuses as high as the sacral prominence are plainly shown, the early discovery of which could have saved the patient the six useless operations and nine years of invalidism. This fact was corroborated further by the most satisfactory result obtained from the bismuth paste injections. It required three months' treatment, but finally the sinuses healed. The sinuses were intrarectal, but the large gaping opening permitted their being easily seen and injected without much difficulty. A year after the cessation of discharge a plastic operation for the incontinence was tried, but resulted in only partial success.

DIAGNOSTIC ERRORS

Other diagnostic errors are frequently discovered by means of the bismuth paste injections, of which the following is an illustration:

FIG. 7.



Paste injection locating unsuspected origin of sinus opening at the hip.

40

R. K., 13 years old, with tuberculous family history, was well until the age of five, when a swelling in his left hip, posterior to the greater trochanter, appeared. An abscess ruptured spontaneously and a copious purulent discharge persisted for seven years, which greatly debilitated the boy. In July, 1908, he was given the first injection of bismuth paste by Dr. Dahl, with whom I saw the case. The radiograph (Fig. 7) disclosed the fact that the abscess did not originate in the hip-joint, as one would suspect from the location of the sinus, but that it communicated with the original focus in the sacrum by a narrow channel. This case proved to be not only an interesting example of the diagnostic value of the bismuth paste, but it likewise credited the therapeutic account with a cure of which both the doctor and patient are justly proud.

A number of similar instances in my experience could be quoted, but space forbids a report of them. This case, however, is a striking illustration of the importance of a correct diagnosis before an operation is undertaken, and also of how easily a correct diagnosis may be made by this procedure. With our experience in using the bismuth paste for diagnostic purposes, we cannot too strongly urge its use.

THERAPEUTIC APPLICATION

The technic in the application of the bismuth paste for curative purposes is practically the same as that used in the diagnostic method. However, in some cases the injections must be repeated.

In my previous publications, and by demonstration of many cases before various medical societies, I have shown that a large percentage of chronic suppurative sinuses, such as result from spondylitis, hip-joint disease, tuberculous kidney, empyema, etc., many of which were considered hopeless, could be cured by this simple and comparatively harmless method, namely, the injection of the bismuth paste.

The injections for diagnostic purposes first employed by my brother, Carl Beck, led me to observe their curative property. In many reported cases the results were so striking, and the instances so numerous, that the possibility of accidental healing must be excluded. In some cases which were considered hopeless, having existed for years, the sinuses closed after the first injection; others,

again, would not heal in spite of the fact that they were of quite recent origin.

My original report, made in January 1908, which comprised a series of fourteen obstinate cases, with ten cures, was a surprise even to those who saw the cases at the meeting. At the present time, two years later, thirteen cases of this series are perfectly well. Surgeons in America and abroad have demonstrated that equally good results can be obtained by others.

In a review of the literature by Dr. Baer of Johns Hopkins University¹⁵ in May, 1909, he makes comparative studies as to the percentage of cures obtained by various surgeons.

¹ Ochaner	20 cases.....	55 per cent.
² Ridlon and Blanchard.....	17 cases.....	53 per cent.
³ Beck, E. G.	192 cases.....	64 per cent.
⁴ Robitschek	9 cases.....	55 per cent.
¹⁰ Don, Edinburgh	17 per cent.
¹¹ Rosenbach, Berlin	50 per cent.
¹² Dollinger, Budapest	12 per cent.
¹³ Beck, Jos. C. (accessory sinus) ..	319 cases.....	22 per cent.
¹⁴ Pennington (rectal fistula)....	17 cases.....	76 per cent.
¹⁵ Baer, Baltimore	12 cases.....	33½ per cent.

The results obtained vary from 12 per cent. to 75 per cent. of cures in the hands of various surgeons. Cases not cured were still under treatment.

Since this review additional reports have appeared in the literature with results even more favorable.

At this point many readers will ask the question, "Why do some surgeons obtain such excellent results and others only mediocre ones?" This gives me the opportunity to suggest, at least, to what the failures may be due.

CAUSES OF FAILURE AS DETERMINED BY INVESTIGATION

In the last twelve months most of the cases which have been treated by myself and my brothers, Drs. Carl and Joseph C. Beck, were cases in which other physicians had tried this method and had for some reason failed to obtain the desired results. Thus we were afforded a good opportunity to study the causes of failure in quite a variety of most interesting cases. The citation of a few examples will be instructive in bringing out the causes of failure.

Foreign Body.—W. W., four years old, one month following an attack of croup in December, 1907, became suddenly ill with chills and fever and pain in the upper arm. Within two weeks of continued intermittent rise of temperature up to 104.5° , a swelling midway between the shoulder and the elbow appeared. Diagnosis—osteomyelitis. A half pint of pus was evacuated through three incisions from shoulder to elbow. The suppuration failed to cease within a reasonable time, and another operation was performed in which a considerable amount of necrosed bone was removed and the entire length of the medullary shaft of the humerus was curetted. Five weeks later the discharge still persisted. At this time the bismuth paste treatment was tried by the physician in charge, but it seemed to be of no benefit. Therefore, another radical operation was undertaken and more necrosed bone removed. Bismuth paste was again injected and after a sufficient trial it was discontinued. In July, 1908, the boy was brought to Chicago for the bismuth treatment. The radiograph here shown (Fig. 8) explains the cause of failure. The tip of a probe, $1\frac{1}{2}$ inches in length, was lodged in the shaft of the humerus. After its removal the bismuth paste was injected and all sinuses promptly closed without a recurrence.

Foreign Body.—J. N., 14 years old. Developed an osteomyelitis in the upper part of the humerus and the tibia four years ago. After the usual treatment at home, which included curettage and drainage of the bone cavities, there appeared to be no tendency to healing. The sinuses continued to discharge pus profusely. He was then brought to me for the bismuth treatment.

A radiograph of the humerus taken before the injection of bismuth paste (Fig. 9) clearly shows what appears to be a sequestrum. In the presence of a sequestrum the injection of the paste would be of no avail, so I proposed a thorough curettage before injection. During the operation I noticed a dark striated object lying within the shaft of the humerus. It was resilient, like a large blood-vessel, and upon extraction proved to be a piece of rubber tubing $2\frac{1}{2}$ inches long. Bismuth paste would no doubt have been a failure had we not discovered the foreign body.

Fig. 10 demonstrates that the paste did not reach the bed of the foreign body before operation.

These two cases represent accidents, and cannot be taken as examples of frequent causes of failure, but the disease itself very often leaves a foreign body at the seat of trouble, namely, the sequestrum.

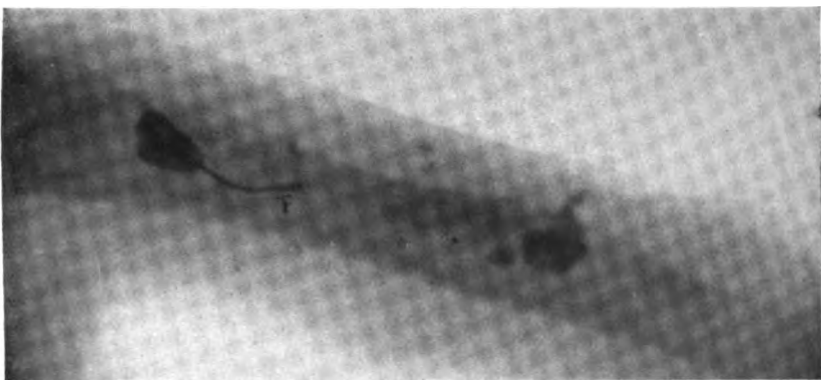
Sequestra are the most frequent causes of failure. Their diagnosis has been carefully studied by my brother, Dr. Carl Beck, who satisfied the members of the Surgical Society of Chicago that sequestra, when present, *can* be recognized by means of the radiograph, practically in all cases. His article on this subject will soon be published in *Surgery, Gynecology, and Obstetrics*. When a sequestrum is present, we do not expect a cure until the sequestrum has been removed. Nevertheless a risky operation should be undertaken only as a last resort. I know of at least two instances in which sequestra have healed in during the bismuth paste treatment.

Faulty technic is no doubt a very strong factor in failures. I have been surprised a number of times, when a case was referred to me in which the paste had been used "faithfully" for months without success, that my first injection should close up the sinus.

UNEXPLAINED CAUSES OF FAILURE

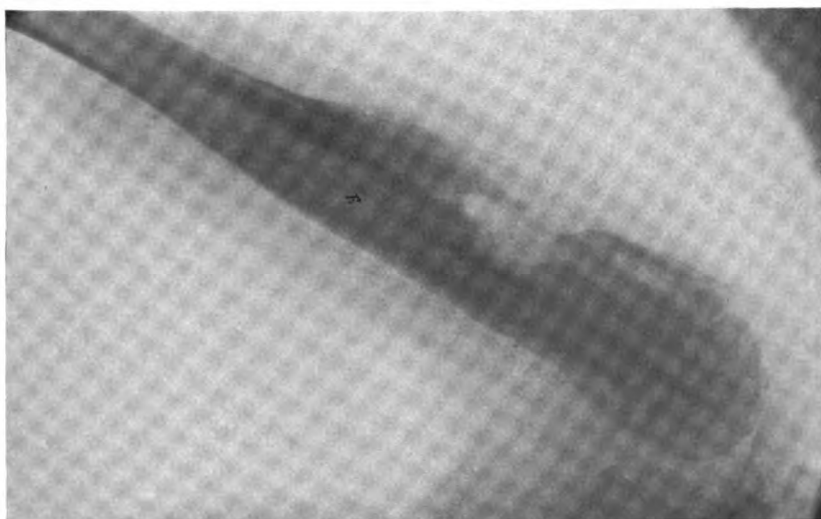
Empyema; Estlander Operation, Closure by Paste.—Miss L. E., 28 years old. Her family and personal history are negative as to tuberculosis. Four years ago she developed an acute pleurisy with effusion. Two weeks later purulent fluid was aspirated, whereupon a resection of one rib was performed and drainage instituted. For eighteen months a copious, purulent discharge persisted. A second operation was performed for the purpose of establishing a counter-drainage, but this also failed to stop suppuration. As a last resort an extensive Estlander operation was performed; but even this radical procedure did not suffice to stop the discharge. The bismuth injections were then tried at home (in Montana) and while the discharge became more scanty and less purulent, it did not cease. Retention with fever often occurred. With this history the patient arrived at our hospital in October, 1909. A radiograph here shown (Fig. 11) gives a vivid illustration of the true condition within the chest which exists after an Estlander operation. The paste occupies the remaining cavity. The upper part of the lung is perfect and functioning. I produce this cut stereoscopically

FIG. 8.



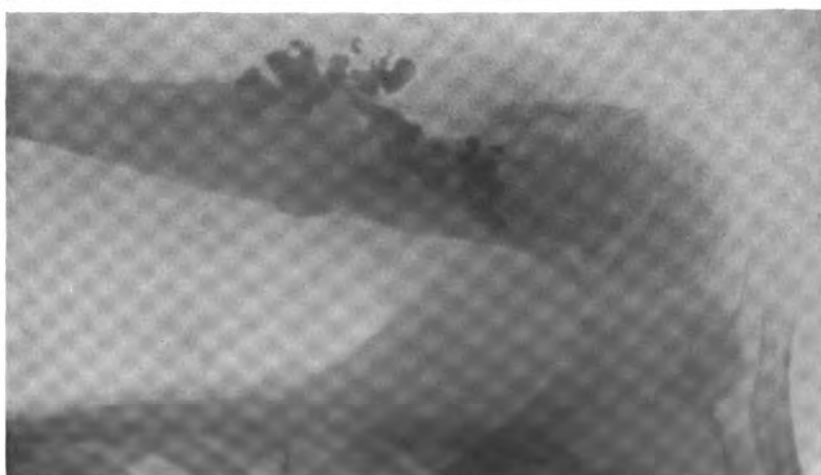
Foreign body (*F*) in the shaft of humerus,
the cause of failure in the paste treatment.

FIG. 9.



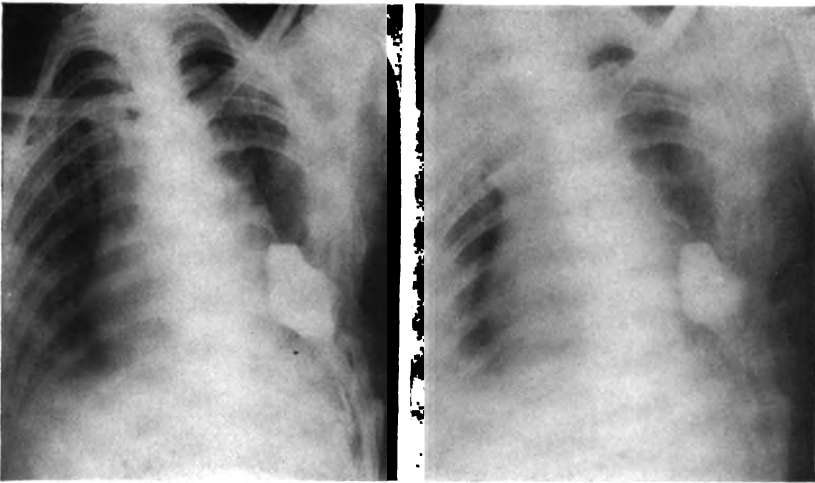
Foreign body (*F*) in the humerus before injection of the
paste.

FIG. 10.



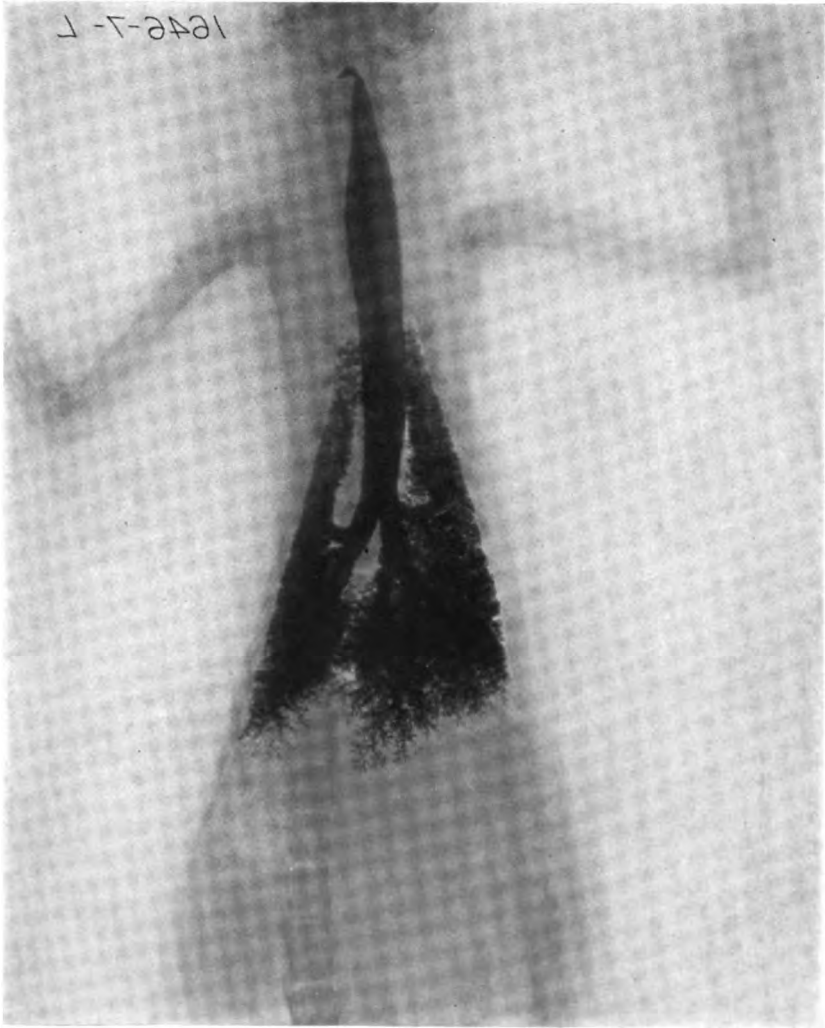
In this case the paste did not reach the back of the
foreign body.

FIG. 11.



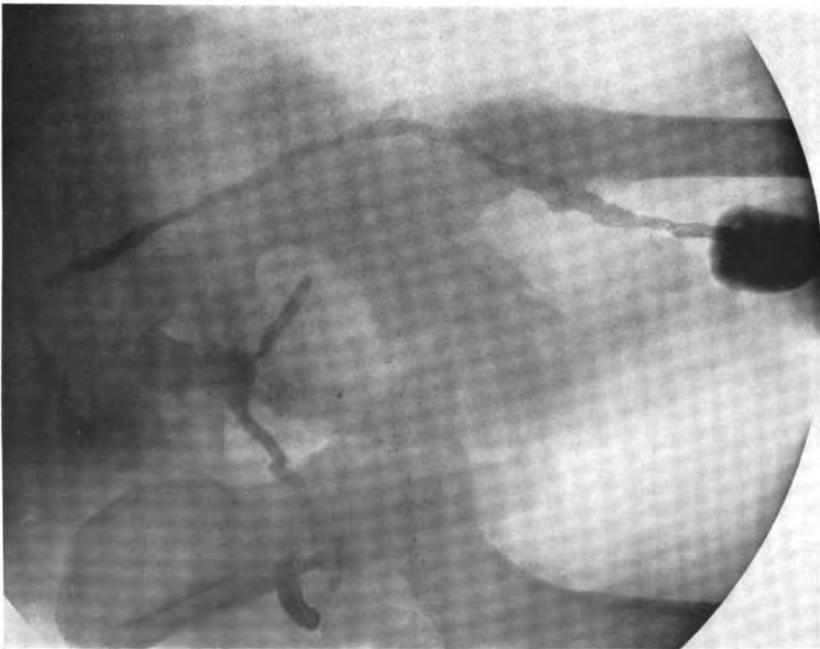
Stereoscopic empyema; Estlander operation two years ago; closure by paste treatment. (This is a negative plate and should be compared with the positive illustration, Fig. 3.) This picture may be viewed as directed for Fig. 3, but shows up better with uncrossed disparity than crossed: Hold the picture in a good light and keep the eyes fixed on the finger-tip, which is first held against the paper and then gradually drawn away from it and toward the eyes until the two views overlap accurately. Dissociation of accommodation and convergence under these conditions will usually require more practice than as described under Fig. 3.

FIG. 12.



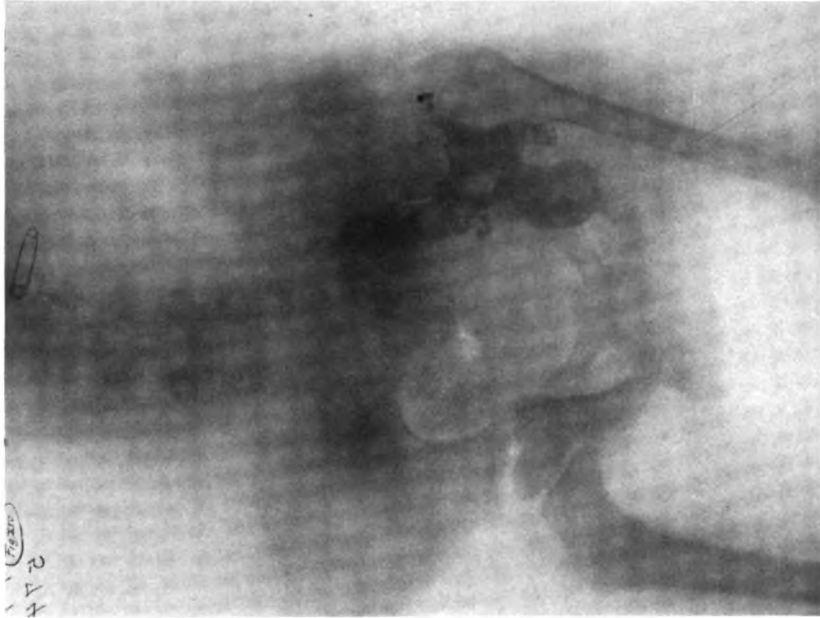
Bronchial tree of cat injected with bismuth paste, showing that paste will penetrate all crevices.

FIG. 13.



Spondylitis, 16 years duration of sinus, closure after three injections of bismuth paste.

FIG. 14.



Prophylactic method of paste injection in tuberculous abscess of hip joint disease.

in order to illustrate the advantage of this method over the single non-stereoscopic plate.

The paste which was in the chest cavity was washed out with olive oil, and the following day a fresh injection of bismuth paste, No. 1, was made. The secretion became sterile, and the sinus closed within one week and has remained so to date. There has been no elevation of temperature or discomfort, and a radiograph taken recently shows the absorption of the paste and the distension of the lung. These are signs most promising for the permanency of the cure.

The underlying principle must always be kept in mind, that the bismuth paste must be soft enough to permit its flowing to the remotest parts of the channels and filling every one of them completely. If a small side-pocket or branch of a sinus is missed, the suppuration will continue and in time the entire tract of the sinus become reinfected. It is not necessary to use great force. Gentle pressure of the piston will suffice to force a liquid paste into these sinuses. This is clearly shown in Fig. 12, *an injected bronchial tree of a cat*. By using undue force one might tear the blind sinuses and force the pus into a fresh wound, which might become a very serious matter.

We have noticed that there are two classes of cases: one class responds promptly to the bismuth treatment, while the other is very refractory. To which class a case belongs is usually decided after the first injection. If the purulent discharge changes into a serous one, a good result is to be anticipated and a closure usually follows the first injection. If the discharge remains purulent, the outlook is not so promising. The injection, however, is not repeated for at least one week. Only the daily dressings with frequent microscopical examination are carried out. Thereafter, the sinus is reinjected every three or four days for a reasonable length of time, about a month. If no improvement is noticed the cause of failure is searched for.

In about 75 per cent. of the failures we have been able to clear up the cause and in one-half of this number a cure was obtained after the cause was discovered.

Another factor which may play an important rôle is the *quality of the bismuth subnitrate*. Dr. Baer, of Baltimore, has advanced

the theory that the subnitrate is hydrolyzed by the heat of the body and free nitric acid is given off, which is most probably the curative agent. He supports his theory by a striking incident.

He treated two series of cases at two different hospitals. All his cured cases were at the Union Protestant Infirmary. At the Johns Hopkins Hospital he and Dr. Kennard could not obtain a single cure. Dr. Dunning of Johns Hopkins University undertook the work of determining whether there is any difference in the way hydrolysis takes place at the body temperature in preparations of bismuth subnitrate from various manufacturers. The results of his investigation have been striking. No two preparations give off the same amount of nitric acid at a given temperature; in fact, some of the preparations hydrolyzed from 5 to 10 times as rapidly as others. This may account for some of the failures in which a preparation is used in which very little nitric acid is given off, or where, by excessive heat, the nitric acid has evaporated. This theory seems plausible and is an inviting subject for confirmation.

With improved technic, the proper bismuth preparation, and increased experience in the diagnostic method and the prevention of bismuth poisoning, our results will certainly become more uniform, and to this end this dissertation is presented.

THERAPEUTIC AND DIAGNOSTIC POSSIBILITIES

Spondylitis of Sixteen Years' Duration.—J. C., 18 years old, with a tainted family history as to tuberculosis, was a strong baby until he had spinal meningitis when eighteen months old. A year later a deformity of spine with all the symptoms of tubercular spondylitis developed. He was under the care of Professors Senn and Murphy for a period of ten years, during which time various immobilizing appliances, casts, etc., were tried, but nevertheless a psoas abscess formed and opened in the right Scarpa's triangle. An irritating pus discharge has persisted for the past twelve years. I made the first injection of bismuth paste in this case in May, 1909, and the radiograph taken (Fig. 13) disclosed a most tortuous fistula, the paste having reached the seat of the focus in the vertebra, and from there being forced into an existing channel on the opposite side which had its blind end about two inches above the hip-joint. There was not the slightest suspicion that this left sinus existed

until it was discovered by means of the paste injections and radiography.

The most pleasing phase of this case, however, was the surprising therapeutic effect resulting from the bismuth paste. With only two subsequent injections the sinus closed, the patient gaining fourteen pounds in weight in four weeks. He is at the present time in perfect health and employed.

In my series of cases there are quite a number of parallel examples, each case having an interesting feature, but space will not permit me to recite them all.

While we have considered it a great advantage to close some of these resistant suppurative sinuses and empyema, we have also gone a step further and instituted a "*Prophylactic Treatment*," a prevention of the sinus formation.

It consists in the opening, under asepsis, of cold abscesses and instead of introducing a drainage-tube or gauze, injecting at the time of incision not more than 100 Gm. of a 10 per cent. bismuth-vaseline paste, without sealing the opening. The paste escapes from the opening into sterile dressings and a secondary infection is prevented. The method has been applied by us during the past eighteen months with almost uniformly successful results, the opening closing in from one to three weeks. Temperature usually remains normal. As an illustration, I quote the following case:

Prophylactic Method in Hip-Joint Abscess.—Master E. T., 7 years old, at the age of $2\frac{1}{2}$ years fell and soon after developed an abscess in his hip. After one year's duration the abscess was incised and drained by his physician. A shortening of three and one-half inches resulted and the sinus closed after a few months, but soon reopened and continued to discharge purulent material for two years. I made the first injection of bismuth paste in April, 1908, whereupon the sinus closed, and with the aid of a high shoe the boy could run about as well as his healthy comrades. In September, 1909 (sixteen months after closure, during which time he had perfect health) he fell down stairs, and developed chills and a temperature of 103° . For three weeks his hip was treated with liniments, etc., but an abscess formed and great tenderness and fever persisted. The boy became greatly emaciated and feeble, and was again brought to me for treatment. On October 24, 1909, the

prophylactic method of bismuth treatment was practised as follows: An incision was made through the gluteal muscles reaching a deep abscess. Without any scooping, or the introduction of any gauze, the resulting cavity was filled with 10 per cent. bismuth paste. The radiograph (Fig. 14) illustrates the size of the cavity. Pain and fever disappeared twenty-four hours after injection, the secretion changed from pus to serum, and the cavity became obliterated; the sinus is now closed. The patient has regained his weight and strength, and runs without crutches.

PREVENTION OF BISMUTH POISONING

It must be admitted that the application of the bismuth paste is not entirely without danger. The slow absorption of the metallic bismuth from large cavities, where large quantities have been retained for a long period, causes symptoms of poisoning similar to those of mercurial intoxication.

The first symptoms, a slight lividity of the skin, appears during the third week. Later we find small blue ulcerations of the gums and back of the wisdom teeth, and a black discoloration underneath the tongue. Soon thereafter patient complains of nausea, headache, and frequently diarrhœa. The urine contains epithelial casts and some albumin. If the progress is not checked, the ulcerations will enlarge, the teeth become loose and the patient becomes cyanotic and begins to lose considerable in weight, and finally may succumb to the effects of poisoning.

In a résumé, Reich of Prof. Bruns's clinic has collected from the literature thirteen cases of bismuth intoxication, of which six cases terminated fatally and seven recovered. This series includes the three cases which I have reported but which, however, occurred in the practice of other physicians who called me to see them. The remaining three cases were those of Kaufman, Cook County Hospital,¹⁶ Eggenberger,¹⁷ Reich.¹⁸

My brothers and I consider ourselves fortunate in not having had a fatal case in our large series, especially so as we had no one to put us on our guard against such a contingency. Luckily we discovered the onset early enough in a case of empyema to prevent a fatality and from this lesson we learned to anticipate and prevent its occurrence.

The prevention consists of not allowing large quantities of the paste to remain in the body for absorption and constantly watching for the symptoms previously mentioned. Should the symptoms appear, the paste should be removed by washing out the cavity with warm olive oil. The sterile oil is injected and retained for twelve to twenty-four hours in order to produce an emulsion which should be withdrawn by means of suction. After its removal all symptoms will promptly disappear. Scraping out the paste with a scoop is a dangerous procedure because it opens fresh channels for absorption.

The following case illustrates the *prevention of bismuth poisoning*:

Mr. R. W., age 33 years. Some relatives have died from tuberculosis. Patient fell from a horse at the age of fifteen, injuring his left hip. Three months later an abscess developed which, after another three months, ruptured spontaneously. Within a year the limb shortened four and one-half inches and five sinuses about the hip developed and persisted in discharging pus for the next seventeen years. In the fall of 1908 the bismuth injections were begun at his home in Colorado. The first few injections were made by his physician. Thereupon, living in a rural district, the treatment had to be continued at home by the patient's wife. She faithfully injected large quantities every day, and after thirty days he developed typical signs of bismuth absorption, namely, blue ulcers of the gums, headache, loss of weight, etc. The radiograph (Fig. 15) demonstrates that enormous quantities of paste have accumulated in pelvic cavities with no outlet for their return and thus absorption took place.

The sinuses were immediately injected with warm olive oil and within twenty-four hours nearly all the paste was withdrawn by means of a suction pump. Symptoms of bismuth poisoning subsided within four days, but the sinuses continued to discharge. Four weeks later I injected 30 Gm. of paste. The result was a change in the secretion from that of pus to serum. Two weeks later the sinuses closed. At this writing (four months after closure) I have received no notice of recurrence.

UNSUITABLE CASES

It is needless to say that even aside from the causes usually responsible for failures there are some cases which will not yield to the bismuth paste treatment. In our own series we found that 6 per cent. could not be benefitted after a persistent treatment of at least one year's duration. In no case do we give up hope of an ultimate cure until after at last one year's treatment.

Occasionally we encounter a case in which treatment is not even worth trying. The following case is an example:

Mr. M. F., 26 years old, developed at the age of 10 a tuberculous knee. In spite of the most skilful treatment, the joint had undergone abscess formation, leaving the joint ankylosed with eight sinuses suppurating for sixteen years. The entire limb had undergone extreme atrophy and a shortening of $6\frac{1}{2}$ inches, so that even though there had been no sinuses the limb would have remained useless.

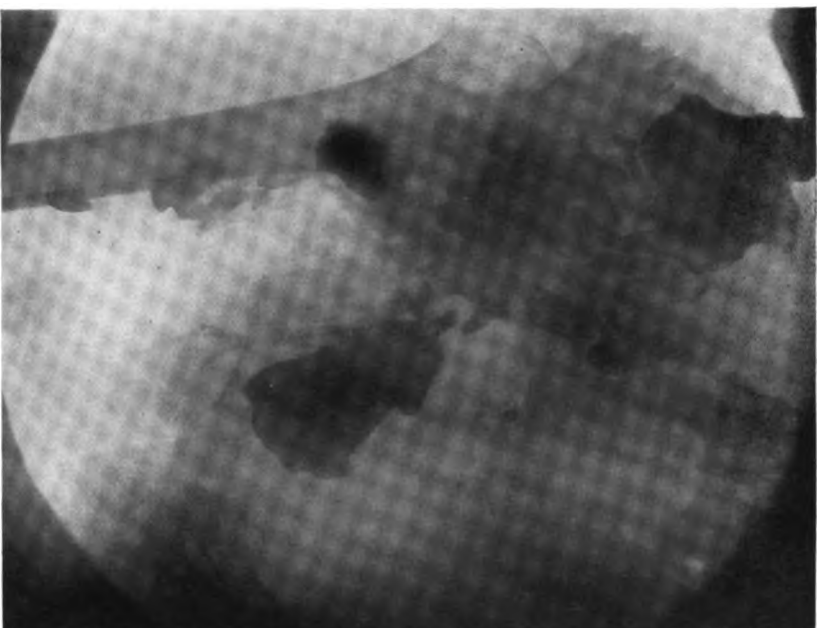
A radiograph, taken after an injection of the paste, for diagnostic purposes (Fig. 16) discloses the hopelessness of a cure. Therefore, I amputated the limb above the knee and had it replaced with a useful artificial limb. The discarding of crutches, a gain in general health and a great improvement in appearance were the benefits derived from this procedure.

LIMITATIONS

To those who have employed the bismuth paste, new possibilities for its application will suggest themselves. The fact that chronic suppurations are so prevalent in so many organs of the body enlarges the scope of its application. Its use in chronic suppuration of the accessory sinuses of the nose, chronic middle ear diseases, mastoids, etc., has been thoroughly tested by my brother, *Joseph C. Beck*. His first report of 319 cases was given a year ago to the Chicago Medical Society. Since then he has treated a large number of cases and a report of his further experience with improved method of application will appear in the near future in the *Annals of Otology, Rhinology, and Laryngology*.

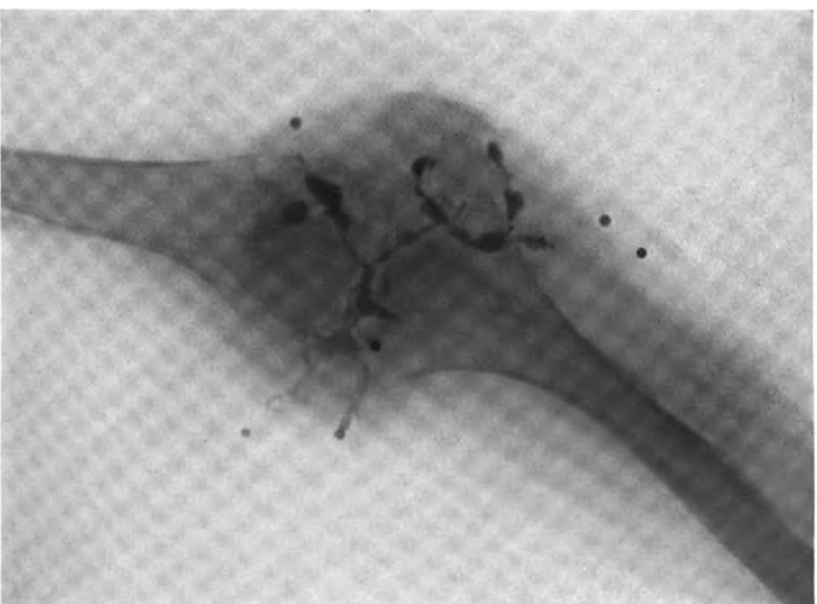
From my personal observation of his cases and with his permission I am authorized to make the advance statement that his

Fig. 15.



Sinuses of hip-joint filled with large quantities of paste causing bismuth poisoning; paste removed with olive oil; recovery.

Fig. 16.



Tuberculous knee-joint with extreme atrophy of limb and eight sinuses; incurable with paste treatment; amputation.



results are surprisingly favorable. The technic in his class of cases is, however, more complicated and can be carried out to advantage only by those who are accustomed to treat these affections, and therefore its use will be limited to specialists.

In fecal fistulæ, following abdominal operation, splendid results may be obtained, providing the mucous membrane of the bowel does not protrude; in other words, if a connective-tissue channel exists between the opening into the bowel and the external opening of the fistula. If the mucous membrane reaches to the skin, it is useless to try it. An operation is the only advisable procedure.

Fistulæ following resection of tubercular kidney have given us the most satisfactory results. Of eight cases treated, seven closed, one of the seven having discharged pus for nine years. Some of these patients have doubled their weight. In one case the kidney was not removed, nevertheless, the sinuses closed a year ago. Patient gained fifty-nine pounds.

The treatment of empyema and lung abscess by this method is so important that a few remarks would be of little benefit and as I have treated this subject extensively in a paper published in the *Journal of the American Medical Association*, as late as December 18, 1909, I refer to that article.

Dentists have already taken up, and with some enthusiasm, the treatment of sinuses about the jaws and also pyorrhœa alveolaris by means of the bismuth paste. The subject was introduced to the dental profession by my brother, *Rudolph Beck, D.D.S.*, a year ago¹⁹; and was recently brought before the National Dental Association in Birmingham by *Prof. Brophy*.²⁰ Judging from the discussions of the subject, the dentists have likewise found the method of great usefulness.

The method has also been employed in veterinary surgery. I have communications to this effect from some prominent surgeons of veterinary colleges of this country. Their results have, however, not yet been made known.

CONTRAINDICATIONS

I am frequently asked whether the paste should be injected into tuberculous joints, instead of the iodoform-glycerin emulsion, or instead of the formalin mixture of *Murphy*. My reply is: *No*.

Although in several cases I have employed it with success, in one case I had a failure which taught me the possibility of producing harm. For the present I do not advise it as a safe procedure.

In acute inflammatory conditions, such as acute phlegmon, acute sinusitis, the paste has not proven very useful, although some gratifying results have been reported. We have been conservative in its application in acute cases, having occasionally noted an aggravation of symptoms.

Wherever there is a possibility of the paste finding its way into a vein, it should not be used. A drop of the paste introduced into the circulation may produce death by blocking the branches of the pulmonary artery. Therefore, *the hypodermic needle should never be employed to make the injections.*

In biliary or pancreatic fistulæ, or sinuses communicating with the cranial cavity, the bismuth paste is, for obvious reasons, contra-indicated.

While some of these limitations may seem too strict and unnecessarily conservative to those who have already tried the method in such conditions with good results, it is safer by far for the present to limit its use to cases involving no risk, at least until reports from large clinics give us the assurance that even those cases in which I advocate conservatism may be treated with the bismuth paste with impunity.

In the meantime there are still a large number of patients, suitable subjects for the treatment, who are *waiting, waiting, waiting*, for their physicians to be convinced that in this new method of treatment may lie the possibility of terminating long years of suffering. Let us treat these first.

REFERENCES

1. BECK, E. G.: A new method of diagnosis and treatment of fistulous tracts, sinuses and abscess cavities. *J. Am. M. Ass.*, March 14, 1908.
2. *Id.*, Toxic effects from bismuth subnitrate. *J. Am. M. Ass.*, January 2, 1909. *N. York. M. J.*, January 2, 1909.
3. *Id.*, Surgical treatment of tuberculous sinuses and their prevention. *Trans. Sixth Internat. Congress on Tuberculosis.*
4. *Id.*, Diagnose, Chirurgische Behandlung und Verhütung von Fistelgängen und Abscess hohlen. *Beitr. zur klin. Chirurgie*, 1909, Band 62, Heft 2.
5. *Id.*, Some practical points in the application of the bismuth paste in chronic suppurative diseases. *Surg., Gynec. and Obstetrics*, August, 1909.

6. *Id.*, Surgical treatment of tuberculosis, pleurisy, lung abscess and empyema. *J. Am. M. Ass.*, December 18, 1909.
7. OCHSNER, E. J.: Michigan State Med. Soc., August, 1908.
8. RIDLON and BLANCHARD: A new method of treating old sinus. *Jour. of Orthopedic Surgery*, September, 1908.
9. ROBISCHEK: Beck's bismuth paste treatment of sinuses. *Northwestern Lancet*, February 15, 1909.
10. DON: *Edinburgh Med. Jour.*, February, 1909.
11. ROSENBAACH, FR.: Zur Wismutbehandlung nach Beck. *Berl. klin. Wchnschr.*, February 15, 1909.
12. DOLLINGER, BUDAPEST: Gümös eredetű tályogok és sipolyok bismuth pastával, E. G. Beck. *Orvosi Hetilap*, 1908.
13. BECK, JOS. C.: Bismuth paste in the treatment of suppuration of the ear, nose and throat. *J. Am. M. Ass.*, Jan. 9, 1909.
14. PENNINGTON: Bismuth paste in the treatment of rectal fistulae. *Lancet Clinio*, December 26, 1908.
15. BAER: Some results of the injection of Beck's bismuth paste in the treatment of tuberculosis sinuses. *Johns Hopkins Hosp. Bull.*, October, 1909.
16. DAVID and KAUFMANN: Bismuth poisoning. *J. Am. M. Ass.*, vol. lii, No. 13.
17. EGGENBERGER: Wismutvergiftung bei Injectionsbehandlung nach Beck. *Centralbl. f. Chirurgie*, 1908, S. 1309 and S. 1537.
18. REICH, A.: Über Vergiftungen durch Beck'sche Wismutpastenbehandlung. *Beitr. zur. klin. Chirurgie*, 1909, Bd. lxx, Heft 1.
19. BECK, RUDOLF: *Dental Review*, Jan., 1909.
20. BROPHY: Bismuth paste in the treatment of chronic suppuration. *Dental Cosmos*, December, 1909.

TUBERCULOSIS OF THE THYROID GLAND, WITH REPORT OF A CASE

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It is well known that the thyroid gland is rarely invaded by the tubercle bacillus. For many years it was considered the one organ of the body that was proof against this infection. Rokitan-
sky made the positive assertion that it never occurred. Virchow, in his early writings, stated that some antagonistic relation existed between the thyroid gland and tuberculosis, and that the existence of a goitre was proof that the subject was not tuberculous.

As further evidence of this antagonism, Rolleston points out that tuberculosis is common in myxedema when the secretion of the gland is wanting, and never occurs in Graves's disease where hypersecretion is known to exist.

As late as 1890, James Berry stated before the London Pathological Society that he was unable to find a specimen of tuberculous affection of the thyroid in any of the twelve large museums of London, nor in those of Oxford, Birmingham, Newcastle, Edinburgh, Glasgow, Geneva, Berne, or Zürich. He exhibited, however, a specimen showing miliary tubercles, which had been removed from the body of a patient who died of general miliary tuberculosis.

The first case recorded was that of Lebert, in 1862, in a woman of twenty-five, who died of acute miliary tuberculosis. He found in the thyroid numerous miliary tubercles. Otherwise the gland was not changed.

Soon after this observation was published Cornil and Ranvier (1870) published a similar case, in which miliary tubercles were found in the thyroid in a case of general tubercle infection. Since then cases of this character have been reported by Cohnheim

(Paris, 1870), Weigert (Virchow's Arch., 88), and Fraenkel. The latter found, in addition to the miliary tubercles, caseating nodes, in a case of chronic pulmonary tuberculosis.

The first to record a case of what appears to have been a primary tuberculous infection of the thyroid was Weigert. In this case death from acute miliary tuberculosis resulted from a caseous focus in the thyroid discharging into a vein. At the autopsy a large tuberculous focus, containing liquified caseous material, was in intimate relation with the median thyroid vein, the lumen of which communicated with the cavity of the thyroid gland. No other old tuberculous lesion was found, and no other explanation of the generalization of the disease was apparent.

Under the title of *struma tuberculosa*, Bruns described what he regards as a case of primary tuberculosis of the thyroid simulating closely malignant disease of the gland:

F. E., *aet.* 41, a widow, had had from childhood a small, soft goitre, which gradually increased in size, but caused no other trouble until six months before admission to hospital. During this latter period it had grown rapidly and caused much pain and dyspnoea. The patient's general health appeared to be good and she had no cough or expectoration or any other sign or symptom of pulmonary tuberculosis. The thyroid gland was enlarged in all parts; the right lobe formed a swelling as large as a small fist and extended outwards under the sternomastoid and downwards under the clavicle. The tumor was covered by healthy, non-adherent skin. It had an uneven surface and was remarkably firm. The left lobe was soft and only slightly enlarged. In the neighborhood of the right lobe were a few enlarged glands. The larynx was somewhat pushed over to the left. There was slight paralysis of the right recurrent nerve, but the voice was scarcely at all affected. When at rest there was no stridor or dyspnoea, but these symptoms were present on exertion. The recent rapid and painful growth, together with the remarkable firmness and irregularity of the tumor and the enlargement of lymphatic glands led to the suspicion of malignancy. Extirpation of the right lobe of the tumor was performed without any difficulty on August 12, 1892, and the patient made a rapid recovery, leaving the hospital ten days after the operation.

The half of the thyroid that had been removed was of firm consistence and had a somewhat nodular surface. On section it was seen to consist chiefly of a homogeneous, gray, firm tissue, in which were embedded a number of isolated masses. These masses were of two kinds: Numerous small circumscribed nodules up to the size of a bean, chiefly near the periphery, representing remains of thyroid tissue, partly unaltered, partly having undergone colloid degeneration, and several dry, yellow masses of the size of walnuts, which had the appearance of unsoftened, cheesy masses like those observed in the so-called granules of large-celled tuberculous lymphomata. At the lower horn of the lobe was a collection of lymphatic glands of the size of cherries, loosely united by connective tissue.

The microscopical examination of Dr. Baumgarten showed tuberculous tissue, with the usual epitheloid and giant cells.

On November 2, 1892, the patient returned with an enlarged lymphatic gland in the neighborhood of the scar. This gland was removed and showed "typically tuberculous" tissue. No tubercle bacilli were found either in the primary growth or in the gland.

Two other cases of primary tuberculosis of the thyroid are reported, one by Clairmont, in which a child of two years, otherwise healthy, suddenly developed a swelling in the neck, which in the course of two weeks reached the size of a small orange. As the tumor rapidly increased in volume dyspnœa, which was slight at first, became alarming. The child became restless and developed a cough. The tumor, situated just above the sternum, was soft and fluctuating, and apparently painful to touch. Aspiration yielded a grayish, thick, puriform fluid. The mass was then incised and curetted. This gave relief as far as the urgent symptoms of dyspnœa were concerned, but the child did not gain in health and a fistula discharging a thin pus remained. Two weeks later the open operation for the removal of the diseased tissue was attempted, but had to be abandoned because of hemorrhage. Six months afterwards, removal of the lateral half of the gland by Von Eiselsberge was successfully carried out. The wound, which had been packed with iodoform gauze, gradually closed by granulation. Microscopic examination of the tissue showed typical tuberculous lesions. No evidence of other tuberculous disease existed.

The other case was reported by Lenormont. In the latter a cold abscess developed in one of the lobes of the thyroid, which was treated by drainage and curettage, and subsequently by partial thyroidectomy.

Although we find in the literature at the present time a number of cases of the nodular type of tuberculosis of the thyroid gland reported, most of them are secondary to some focus in a neighboring organ.

Grassert and Estor (cited by Lenormont) report a case where a large caseating focus developed in the thyroid secondary to a cervical Pott's disease. The infection reached the thyroid by way of the lymphatics.

Berard cites a case where a tuberculous abscess of the thyroid was consecutive to a laryngeal tuberculosis.

In Fraenkel's case a large tuberculous abscess developed secondarily to a spinal tuberculosis. This abscess opened and discharged into the œsophagus.

From a surgical standpoint, only the nodular or caseating type of tuberculosis is of importance; the miliary form is found only at autopsy. In this, the former type, the rapidity with which the tumor grows often suggests malignant disease, as in Bruns's case, while with the increase in size of the tumor grave compression symptoms early call for surgical interference. The nodular character of the tumor, the hard consistency, the adhesions of the gland to surrounding structures, all simulate, as do the rapid development of pressure symptoms and the enlargement of the neighboring lymphatics (Bruns's and Fraenkel's cases), the characteristics of malignant growths. With the development of tuberculous abscess or the formation of fistulæ, the nature of the disease is made clear.

The following case came under the author's observation during the last year:

Miss G., aged 28. Entered St. Luke's Hospital, May 24, 1909.

History.—Present illness began about one year ago, when she first noticed a swelling in the neck to the left of the median line and midway between the chin and the sternum. At this time she consulted a physician, who told her she had a goitre and prescribed the local application of iodine. The treatment did not improve the condition and was soon abandoned. The swelling gradually in-

creased from the size of a walnut to that of a small orange. About a month ago it began to cause pain, dyspnoea, and difficulty in swallowing. Poultices were applied and after several days an opening formed, through which was discharged thick pus. Since then, at intervals of a few days, large quantities of pus and cheesy material have been discharged, without materially lessening the size of the tumor.

Examination on admission showed a well-nourished, healthy-appearing young woman. The temperature and pulse not above normal. Lungs, heart, and kidneys were normal. In the lower part of the neck, to the left of the median line, was a swelling as large as a small orange, which was firm and nodular to touch and not especially painful. The skin, excepting where the fistula presented, was normal in appearance. The tumor was not adherent to the surrounding structure and moved upwards and downwards with the act of deglutition. Upon introducing a probe into the fistulous opening, it could be made to enter about one and one-half inches, backward and toward the median line of the neck. The fistula led to a small cavity that could not hold over a teaspoonful of fluid. The cavity was filled with bismuth and vaseline paste, which was forced in through a syringe. In this manner four ounces of paste was made to disappear. Just where it went to was a matter of doubt until an X-ray picture was made. This showed a cavity fully four and one-half inches in length, and with a diameter that would about equal the index finger, passing down behind the sternum.

On the first of June, the tumor was exposed through a transverse, curved incision. It was found to be the left lobe of the thyroid, enlarged by an inflammatory process. In the centre of the mass was a cavity, the size of a filbert, lined with granulation tissue and containing cheesy material and pus. The left lobe was separated from the surrounding structures and removed. The fistula was found to lead from the cavity in the mass and pass through the posterior part of the capsule of the gland and down behind the sternum for a distance, as measured on a probe, of five inches. After thoroughly swabbing out the cavity, it was packed with iodoform gauze and the wound in the skin closed by suture. The wound healed quickly, but the fistula remained

after removing the gauze. This was treated for two weeks by repacking, after filling the cavity with iodoform emulsion of 10 per cent. strength. At the end of this time it had diminished in size until it would just admit an ordinary flexible uterine sound and the discharge had nearly ceased. It was then filled with bismuth paste, upon her own request, and the patient discharged and returned to her family physician for further care. From him it was subsequently learned that she had returned to her home in Europe before complete closure of the fistula was accomplished.

Examination of a cut section of the mass showed the remaining part of the gland was beset with small nodules, from the size of a pinhead to that of a pea. Some of these present in the centre, areas of cheesy degeneration. The large cavity in the centre was partially filled with cheesy matter and presented upon its walls miliary tubercles of a grayish-yellow color.

Histologically, these corresponded to tuberculous deposits. No tubercle bacilli were found.

BIBLIOGRAPHY

- BERARD: LeDentu et Delbet, *Trait. de Chir.*, 1900.
- BERRY: *Tr. Path. Soc.*, Lond., vol. xli, 261.
- BRUNS: *Beiträge zur klin. Chir.*, Bd. x.
- CHIARI: *Med. Jahrbuch*, 1878, 69.
- CLAIRMONT: *Wiener klin. Woch.*, 1902, No. 48.
- FRAENKEL: *Virchow's Arch.*, Bd. civ, 58; *Berliner klin. Woch.*, 1897.
- LEBERT: *Die Krankheiten der Schilddrüse*, 1862, Bd. ii.
- LENORMONT: *Arch. gen. de Chir.*, March, 1909.
- PERRY: *Tr. Path. Soc.*, London, vol. xlii, 298.
- ROGER et GARNIER: *Arch. gen. de Med.*, t. 3, 1900.
- ROKITANSKY: *Lehrb. der path. Anat.*, Bd. iii.
- ROLLESTON: *Tr. Path. Soc.*, London, vol. xlviii, 197.
- SCHWARTZ: Cited by Berard.
- VIRCHOW: *Die krankhafte Geschwülste*, Bd. iii.

Gynæcology

PROGRESS OF GYNÆCOLOGY AND ABDOMINAL SURGERY DURING THE LAST TWENTY YEARS *

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WHEN one looks back upon the wonderful advances which have been made in our specialty during the last quarter of a century one cannot help being filled with pardonable pride over what it has done, not only for women but also for surgery in general. The writer has never been able to get himself in touch with the mental attitude of those few pessimistic members of it who occasionally write papers on the passing of gynæcology. On the contrary, far from showing any sign of decadence, gynæcology has every right to claim that it is at the very pinnacle of its usefulness and honor. It was our pioneers who first blazed the trail through the then unknown land of local and general peritonitis, so that now not only we but the general surgeon can march safely through it, as through a well-lighted street after dark. When I am able to say, as I can to-day, that cancer can be, and is being, stamped out of every community by the gynæcologist surrounding himself with a band of faithful general practitioners who send to him every case of lacerated cervix, which he repairs, and thereby saves, not only that woman but all of her friends who are suitable to take that dread disease—that one thing alone is enough to make us proud. When we think of the thousands of women who have been snatched from certain death by internal hemorrhage due to ruptured tubal pregnancy, and still more when we consider the hundreds who have been operated on before rupture without any mortality and almost

* Read before the Medico-Chirurgical Society of Montreal.

without risk, nearly all of whom twenty-five years ago would have died either suddenly or by prolonged suppuration, surely we have reason to be proud. When we think of the thousands of women who used to drag out a wretched existence for twenty years, confined to their rooms like prisoners in a jail by reason of a uretero-vaginal, vesicovaginal, or rectovaginal fistula, all of whom to-day are by our art being quickly and surely restored to health and happiness, I cannot understand how any one, and least of all a gynæcologist, can take anything but the most optimistic view of the situation. True, the general surgeon follows closely in our lead and soon reaps for himself and his patients the advantages of our discoveries. To these he is most welcome as long as he sticks to general surgery; but when he tries to be a gynæcologist and does curetting and repair of the cervix, ever so badly, it is time to call a halt, if not for the women's sake at least in the interest of surgery itself. The writer could tell of fifty cases at least where a general surgeon has suffered in reputation and the woman in health by his failure to possess the *tactus eruditus* by which alone an accurate diagnosis can be made.

Gynæcology has suffered somewhat from another cause, namely, the premature entrance into its ranks of many young men without any experience in general medicine, with the result that they try but fail to cure by complicated operations or local applications conditions which could easily be remedied by simple general treatment. It would be a consummation devoutly to be wished if every one who intended to be a gynæcologist would get ten years' experience in general practice before devoting himself to this difficult specialty.

Having cleared the ground of these detrimental questions, all the rest is hopeful and satisfactory. Let us take up for a moment and for a very brief discussion each of the most important advances, first in Gynæcology and then in Abdominal Surgery. First in importance comes the repair of every lacerated cervix as soon as it comes to us and the hunting up by the family doctor of those who do not know enough to come to him of their own accord. Every one must give the credit of discovering the enormous influence for ill borne by a lacerated cervix to Emmett. If we measure a man's life-work by the happiness he has brought to millions his name should never die, and it is only natural that his great discovery

should be best and most often carried to its logical result in the land of his adoption. If the young obstetrician could fully realize what a serious thing it would be for his patient's whole future on earth and for her husband's welfare thereafter to cause a lacerated cervix he would pause and think twice before he applied the forceps to a half-dilated os. He should think of the septic absorption and the arrest of involution and the falling back and down of the heavy uterus dragging the bladder and rectum with it; of the healing by scar-tissue, which is the hot-bed for the parasite of cancer later on; he should think of the obstructed circulation leading to chronic fungous endometritis with its hemorrhages every three weeks and lasting eight days; of the miscarriages on which many women so lightly embark but which in the case of the woman with the lacerated cervix come on repeatedly no matter how much she wants another child. He should think of the great sympathetic nerve that is compressed and irritated until it squeezes almost every drop of blood from the brain and the once beautiful and accomplished creature becomes a mental as well as a physical wreck, often ending her days in the asylum for the insane or filling a suicide's grave. If he thinks of these things and in spite of all goes on and tears the cervix he must take it upon his conscience to see that the damage shall have been repaired within the next few months. During the last twenty-five years all these things have become more generally recognized, so that in many communities there is hardly an unrepaired lacerated cervix to be found. This has had just that most happy result which one might expect, namely, that cancer of the uterus is becoming more and more rare. At least this is my experience and it is borne out by several private communications which I have received from prominent Fellows of the American Gynecological Society. We still hear, but more rarely, the objection raised that it is of no use to repair the cervix of a woman who is likely to have more children,—first, because it will make the first stage of the next confinement much more difficult, and second, it will almost surely be torn again. This was a real objection until Schroeder in Germany invented his operation of amputating the diseased cervix, scar-tissue, cysts, and everted and eroded lips together. There may be seen in the Museum of McGill University a series of these amputated cervixes removed by the writer, some of them as much as three inches long, and when the lips of the os

uteri were spread out, three inches antero-posteriorly, exposing a large amount of ciliated epithelium which was not meant to be exposed to friction as is the pavement epithelium of the vagina. These specimens were removed from uteri as long as six inches, so that they were shortened to three inches and made that much lighter before being ventro-fixated high up on the abdominal wall, or in cases where the bladder was prolapsed anchored by vaginal fixation. This amputation by Schroeder's method, or by a method of my own, almost completely does away with the first stage of labor; for with one or two pains the os opens widely. I always warn the family doctor that he must go at once on being called if one of these cases has another confinement, as even then he will barely get there in time. Emmett's operation as I have sometimes seen it done would almost make another delivery impossible *per vias naturales*.

The next great step has been the more general tendency towards earlier operation. Twenty-five years ago it was the rule for a general practitioner to treat cases of cancer during their first six months by local applications made through a Ferguson's speculum. The favorite application was the solid stick of nitrate of silver which of course only irritated the cancerous growth. I shall never forget the remorse of a conscientious country doctor who had been treating such a case for six months *suspecting but not being sure* that it was cancer all the time, and afraid to tell the patient what he suspected. When I told him that it was cancer but too far advanced by six months to give the woman any chance of her life his regret was pitiful to behold. In those days I had on an average at least fifty-two cases of cancer a year and hardly any of them in an early enough condition to give them any chance of saving their life. Now as all my former students and present brethren as well as many others who send me patients make it their duty to have every known case of lacerated cervix repaired while the women are yet young there are almost no cases of cancer in their practice; while the rare ones that do occur are suspected by them one day, seen by me the next, and have hysterectomy the third day, with the result that we have many women alive and well after from five to ten years. I have seen at least one hundred women die from cancer of the cervix just because their doctor *was not sure* that it was cancer in the beginning, but only *suspected* it; unfortunately he did

not tell the victim so that she might save her life. And this reminds me of another important advance in this connection. Twenty-five years ago it was the custom for a friend or relative to come with the patient at her first visit, and this misguided friend would ask to speak to me privately before the patient came in. What she wanted to say was this: "Doctor, if she has anything serious the matter do not tell her but tell me, as the shock might kill her." I have even had doctors speak to me in this way. But my answer has always been the same,—“The only person who really has a right to know and the principal actor in the tragedy is the victim”; so that now no one makes such a proposition to me. I would advise all young doctors to make a solemn resolution early in their career that they will be absolutely straightforward and truthful when dealing with a cancer patient, so that she may intelligently follow the road to safety; and to be absolutely silent regarding the patient's affairs to everybody else who has no right to know, unless the patient chooses to tell. In time you will get a reputation for veracity which will add greatly to the weight of your opinion in after years. I remember once a woman coming to my office with her mind made up and her operation fee, rather a handsome one, ready. When I examined her I found the whole pelvis filled with a cancerous mass. When I told her the truth, that her case was hopeless, and that no operation could do her any good, she was very angry and said she would find some one else to take her money. I did not think she would; but I am sorry to say she did and was operated on next day. She died the evening of the operation. I was told by the friend who had sent her to me that she spent her last hours expressing her regret over and over again at not having taken my advice, and just because of my course in that case at least a score of her friends have placed themselves in my hands. I lay some stress on this point because even some of our leading authorities on ethics hold a contrary opinion. But how can a woman understand that her very life depends on saving days or hours or even minutes until she is operated on, if she does not know the reason why. Family doctors used to excuse themselves for the six months delay by saying that the patient would not hear of an operation; but I asked them, “Have you told her why? How could she know that every one of those one hundred and eighty

days counted against her when she did not know what was counting?" One might say, "Oh, that is all very true about the operable cases, but when the woman is already inoperable when we first see her why take away all hope?" There are two very good reasons for telling even her. First, she has a right to have all the time possible to prepare her affairs, spiritual and worldly; and second, she has a right to take every precaution to protect those she loves from contracting her sad disease. And this introduces another great advance of which, however, we are only just now on the threshold, namely, the contagiousness of cancer. Thirty years ago the writer published and reported at his medical society case after case absolutely proving that heredity had nothing to do with tuberculosis, but that on the contrary it was a highly contagious and absolutely preventable disease. The proof was only clinical, but was such as any judge or even any high school boy would have accepted as conclusive, provided he had never had any preconceived notions of it. But no such person could be found; for everybody over fifteen had been trained to think that consumption was hereditary and so it has taken thirty years almost to accept a truth which was as true then as it is to-day. Now why, I ask you, must we lose twenty-five years before accepting a truth which is just as evident to an unprejudiced mind? Clinically I *know* that *cancer is contagious and contagious alone*, and that heredity has nothing whatever to do with it. But I have not captured the cancer plant, although I do believe that I have seen it under the microscope. Fifty thousand people died from cancer in one country alone last year and before dying they probably gave the disease to a hundred thousand more. Why do we doctors not shout it out from the housetops that the disease is contagious and save this awful waste of adult life? We have stamped out the plague, cholera, typhus and smallpox, and are stamping out tuberculosis; let us add one more to our self-denying triumphs, and stamp out cancer too.

Not only in the cases of lacerated cervix and cancer but in every other kind of operation are the practitioners, in this district at least and I hope it is the same everywhere, sending their patients earlier so that the mortality from all operations has almost reached the vanishing point when done by the best operators. Fancy one hundred consecutive abdominal sections without a death. And yet

they were done for the same diseases, as they were twenty-five years ago when the best record was 15 per cent. of deaths. It is true we now have asepsis and the Trendelenberg position which have worked wonders, but a very important factor has been the getting of fibroids and ovarian tumors while they are comparatively small and before they have formed dense adhesions with or perforated into the bowel and before they have caused albuminuria and heart murmurs. And in this connection I may mention another great advance from the patient's point of view at least, that whereas formerly even the best operators refused to operate on a patient with disease of the kidneys or disease of the heart we now know that both of these conditions depend upon the presence of the tumor and that within a few months after its removal both heart and kidneys will be working perfectly well. My own experience has borne this out many times.

Another great advance which I have already mentioned is the lower death rate, which has been steadily falling for twenty-five years. Everybody will admit that it is important if possible not to lose our operative cases; but it is more important still than is generally supposed. And the reason is this: when we operate on a hopeless case of cancer, for instance, and the patient dies the same or the next day, we are not only the direct cause of her death a little while sooner than she would otherwise have died, but indirectly we cause the death of many other women whom we have never seen, women whose condition has been recognized by their family doctor early enough to have an operation almost free from risk and which would make an absolute ultimate recovery. These ten or twenty women who could all have been saved if operated on at once are so frightened by the death from operation of their friend or acquaintance that they delay month after month and only make up their minds at last when their cases too have become hopeless. I have been taken to task at a great society meeting for expressing this opinion, one of the less experienced Fellows claiming that I had no right to consider these twenty women who were as yet unknown to me; and that my only concern should be with the case in hand. Technically I may be wrong, but my convictions have saved me from doing operations with a well-established mortality of 75 or 80 per cent. In my earlier years I thought it was a disgrace

to refuse to operate on hopeless cases; now I think it a disgrace to touch them, for the reason above-given. Financially my convictions have been an expensive luxury. I have just completed a very busy six months term of service at the Western General Hospital without a death of any case on which I operated. I have been frequently asked by my post-graduate pupils to what I attribute such a low death rate among so many major operations—a list of which is appended to this article by which you will see that many of them were quite serious. The factors in this result I will now give as I have often given them in my clinical lectures, in the order of importance as they appear to me.

1. Rapid operation consistent with carefulness.
2. The least possible anæsthetic.
3. Better hæmostasis.
4. The Trendelenberg posture.
5. Not seeing, not touching and especially not exposing the bowels.
6. More careful preparation of the patient.
7. Fowler's position and drainage through the vagina in bad pus cases.
8. Getting the cases earlier, and thus having
9. Fewer adhesions, so that there is
10. Less injury to the bowels.
11. Fewer assistants, so that we may have more perfect asepsis.
12. Better suture material.
13. More air and less heat in the operating room.

Each of these factors in preventing deaths deserves a few words of explanation. I sometimes think that we should put the Trendelenberg posture at the head of the list. I can truly say that I never begin a laparotomy without a feeling of intense gratitude to this great but modest German professor. The abdominal surgeons of the world should now while he is alive erect a statue of him in his native town of Leipsic, for we know that without his invention it would be impossible to do a hundred abdominal sections without a death. If any who read this could see a laparotomy done by an expert to-day and then see the same operation as it was performed twenty-five years ago they would only then be able to appreciate how much Trendelenberg's position has contributed towards our low

mortality. In those days there was a long incision made laboriously, layer by layer on a director for fear of injuring the intestine, but as soon as the incision was made the bowels were lifted out, if they did not escape themselves, which they usually did; and for the next hour or two they were constantly exposed and handled; being frequently covered or wrapped up in hot wet towels which in a few minutes became cold evaporating lotions. When this was not done the best they could do was to have one assistant spending all his time in pushing the bowels back into the abdominal cavity; with the result that intestinal paresis and distention were regular sequences of every abdominal section. The first six factors in a low death rate really depend upon the sixth and fourth; namely, careful preparation of the intestines for two days before operation, and the Trendelenberg posture; for by reason of these two the intestines fall back out of sight the moment the first nick is made in the peritoneum. A hot gauze pad is laid over them so that they are not seen much less handled during the rest of the operation. The time during which the peritoneum is exposed is very much shortened. Also the quantity of anæsthetic used is very much reduced; I have done many abdominal sections with less than an ounce of A.C.E. mixture. The third factor, better hæmostasis, also depends largely on the Trendelenberg posture; in former days a terrible hemorrhage would be going on until the patient's pulse disappeared at the wrist, but owing to the bowels being in the way we could not find the vessel from which it was pouring. Now we tie everything before cutting it and if by chance a ligature comes off and bleeding starts we have no difficulty in finding it and putting a stitch in it. The expert operator has a definite plan in his mind, namely, to cut off the blood-supply and get the tumor out; he does not make a single unnecessary movement or say a single unnecessary word until that has been accomplished. His instruments are where he can pick them up without taking the time to think of the name and send the message down to his tongue, and across to the tympanum of the nurse, and up to her brain, and down to her eye, and back to her brain, and down to her hand. All this takes a few seconds which multiplied a hundred times means minutes. In a word, a hundred thousand dollar operating room is only helpful if it enables us to cut five or ten minutes off the time of the opera-

tion. Asepsis can be obtained without it and if it complicates rather than simplifies it must prolong the time and increase the mortality. A few well trained assistants may shorten an operation by several minutes by following the operation a minute ahead of the operator; my assistant, Dr. Lorne Gilday, by many rehearsals, knows what I will want next, and has it ready to my hand a second or two before I need it.

I must say a few words more about the sixth factor, better preparation of the patient, because a great many of my friends from the country and even a few in town, still fail to realize the importance of getting the patient into the hospital two nights before the operation. Many a time, twenty years ago, I have opened the abdomen of a patient, who unknown to me had had a hearty send-off supper the night before, and then been driven over a country road for several hours during the night in order to take the train at 3 or 4 A.M. and who was first seen by me at 9 A.M. I knew that those patients did badly and it hardly seems credible now that any entreaties or threats of the husband or family doctor who came with her, or even of the patient herself, could have induced me to operate on her that same morning. Only in case of perforated appendix or ruptured tubal pregnancy can I be induced to operate the same day on a patient who has not been prepared. Two days and two nights in bed, three hot baths to take off the dead skin full of bacilli, a dose of castor oil twenty-four hours before to clean out the colon bacilli and decomposing food, and the drinking of two or three quarts of water to fill up the arteries and get the kidneys and skin working well: all these contribute very materially towards a quick operation and a low death rate. The seventh great factor, which I would have placed at the head of the list did it not apply to very desperate cases only, is the Fowler position. During the last five years that I have been using it, I have saved practically all the desperate cases which I would otherwise most certainly have lost. It is especially valuable in peritonitis due to perforation of the appendix or intestine, and is especially available in women because it is so easy to pass a quarter-inch perforated rubber tube down through Douglas's cul-de-sac and out through the vagina. It is astonishing what quantities of horrible-smelling pus and serum will drain away from such a case. It has completely changed the

prognosis and indeed the operation; for there is no longer any need to wipe off the intestine; get in and get out as quickly as possible is the new motto; get the appendix off even with the cæcum, and Fowler's position and the drainage tube will do the rest. These were the cases which gave us the high death rate when we closed up and left the disabled peritoneum to attempt this herculean task of absorbing all this pus; or even when we drained, but against gravity. The poisonous fluid was carried all over the peritoneum by the movement of the bowels. Factors eight, nine, and ten all depend upon the general practitioner; if he sends us the cases early there will be no adhesions and less injury to the bowels. The eleventh factor, fewer assistants, has only grown upon me by experience. I believe that it would be in the interest of the patient if I had the same nurse to give the anæsthetic thousands of times, and another nurse to assist me a thousand times. I have had and have now some fine assistants but they all have the one great fault of leaving when they have become most useful. The general practitioner who brought me the case used to feel offended sometimes, when I did not ask him to assist me in a serious case. But now they all understand the importance of team work and for their patients' sakes they are willing to make the personal sacrifice of allowing my regular assistants to give the anæsthetic and help me with the operation. A man in general practice who has to open abscesses and attend cases of puerperal septicemia could make his hands sterile, but it is a serious undertaking. Rubber gloves have somewhat lessened the danger, but they are not infallible.

The thirteenth factor, more air and less heat in the operating room, have had a lot to do with the lessened mortality. I have never seen the operating room yet where three thousand cubic feet per hour were supplied to every person in it. The experience of the Japanese surgeons in their last war has proved conclusively that operations performed in the open field do better than those in an operating room. We no longer see the patient's face bathed in clammy sweat throughout the operation which in the old days was due to advanced carbonic acid poisoning. The tremendous loss of water added to the too free purging with salts the day before and the deprivation of water after the operation had a bad effect upon the case. Now we operate in a room at 70° F. with the windows

open but well protected with fly screens, and many of the patients go out of the operating room with as good a color as when they came in. In fact I attribute a good deal of my success in having no death during my six months of service at the Western to its occurring during the six months of summer when the windows are all open. Twenty-five years ago we would not do an abdominal operation unless the temperature of the room was about 85 degrees. We have almost done away with the terrible thirst from which patients used to suffer, not only by giving them more to drink the day before but also by the mild salt solution enema after the operation, the reservoir being hung only a few inches above the rectum. It is astonishing what a quantity of water can be thus introduced even when the patient is vomiting and can keep nothing on her stomach. I used to suffer acutely for twenty-four hours after a big operation, with pains all over me; a feeling as if I had been bruised and beaten, but I have completely done away with this by drinking two or three quarts of mineral or other water immediately after to make up for what I lost by perspiration. The patients have also been relieved of the bruised and aching feeling by the copious rectal absorption of normal salt solution or artificial serum.

Twenty-five years ago abdominal hysterectomy for fibroid had a death rate of 50 to 60 per cent., but owing to all these advances it now has a death rate of less than five. In many of my cases where the tumor was the size of an adult head or less the loss of blood has not been over an ounce or two. Broad-ligament cysts which used to have a very high mortality can be removed now with less than 5 per cent., by following Howard Kelly's method of going down on the easier side, cutting across at the internal os, and rolling the tumor out of its bed and off the arteries, veins, and ureter. In order to have almost no death-rate both in broad-ligament cysts and in large fibroids the uterus must be sacrificed as well as the ovaries and tubes.

There is one so-called advance which in my opinion has been no advance at all; what is called conservative gynæcology, which does not conserve the health of the patient. About twenty-five women who had had conservative gynæcology done on them by other doctors have come to me for a second operation for the removal of the second ovary which it would have been much better to have

removed at first. I am ashamed to say that I have been induced by the force of professional opinion to do what I knew at the time was an incomplete and useless operation. But the patient wished it so, her husband wished it so, the family doctor wished it so, and the medical society was strongly opposed to what they thought was radical work, but which I felt was necessary to turn an invalid into a healthy, happy woman. As I have often pointed out, the same causes which made the left ovary sick and sore were at work on the right ovary and tube, although the more favorable circulation in the right ovarian vein causes the disease to take a little longer to progress to the point where it makes life unendurable. Let us do all we can by treatment for a year at least to avoid an operation, but if the patient is no better by that time let us then operate and do all that is necessary to make the one operation or set of operations done at one séance a complete success. Let me now give a very brief report of the more important and interesting cases at the Western during my six months' term.

Hospital Number, 5587.—Mrs. D., *aet.* 38, one child. She was sent in for menorrhagia, not painful but coming on every two weeks. For some months she has been complaining of pain in the right side and she cannot sleep on her back. A mass the size of three oranges can be felt in Douglas's cul-de-sac. The appendix is tender on pressure. At operation the tumor proved to be a dermoid cyst which was removed, as was also a bound-down appendix. Good recovery.

Hospital Number, 5599.—Mrs. M., *aet.* 28, two children and four miscarriages. Uterus feels large and sound enters five and a half inches, and the cervix is lacerated. Each miscarriage has left her weaker and weaker. I only mentioned this case to point out that every third or fourth case in my note-books gives the history: "Never well since a miscarriage four years ago—or ten years ago."

Repeated miscarriages when not due to syphilis are generally attributable to fungous endometritis, a varicose condition of the veins of the endometrium. The bad circulation is most often caused by a retroversion, which in turn is the result of subinvolution. The quickest cure is to curette very thoroughly with a sharp curette, apply strong tincture of iodine (Churchill's) and carbolic acid,

equal parts, to the inside of the uterus, and then to pack in firmly a long strip of iodoform gauze. I leave this gauze in for five days during all of which time the uterus is making more or less frantic efforts to expel it, and these contractions are precisely what are needed to bring about involution. Sometimes they are so powerful that it is necessary to give a few hypodermics of morphine to ease the pain. Over and over again I have seen a complete cure result from this treatment; not only did the uterus become normal in size and the flow normal in quantity, but the woman has gone on to full term in her next pregnancy. It is well to lay great stress on the importance of having a child at full term as part of the cure; the uterus gets into a bad habit, so to speak, of aborting and the best way to get it out of this habit is to make it go for once at least to full term. When these cases do become pregnant they should be under our care up to the fourth month, taking viburnum and being temporarily relieved of any displacement by the aid of a pessary. If the subinvolution is due to a lacerated cervix the latter should be amputated after the dilatation and curetting. This was done in the above case as well as in Case No. 5602, Mrs. M., *aet.* 35, mother of two children, one miscarriage. Her elongated cervix projected through the vulva. Also in Case No. 5610, Mrs. G., 23 years old, one instrumental delivery followed by three miscarriages. As she had a history of chronic appendicitis, she had curetting, repair of cervix, and removal of the appendix at the same time.

Case No. 5632.—Mrs. T., *aet.* 35, was sent by Dr. Wattier. As she was a widow and had to earn her own living and had been confined to bed off and on for several months with dysmenorrhœa and chronic appendicitis I removed her ovaries and tubes and appendix on April 14. I have since heard from Dr. Wattier that she made a good recovery and is now working hard.

Case No. 5375.—Mrs. T., temperature 103° after an abortion. Washed out the uterus, applied iodine and carbolic, put in a light gauze drain but did not curette. Curetting in these cases, especially with a sharp curette, is a dangerous proceeding as it opens up many new avenues for absorption of poison. By the gentle means employed in this case she went home in a week with a normal pulse and temperature.

Case No. 5750.—Mrs. M., *aet.* 48, mother of seven children,

two miscarriages, came on May 10 with a fibroid tumor which kept up a severe hemorrhage every month and showed no signs of stopping. The removal of her uterus at the internal os and her tubes and ovaries was a quick and safe operation. As she was fat and flabby a cigarette drain was put in at the lower end of the incision down to the fascia which was removed in thirty-six hours—after draining away an ounce of serum. This little drain is a great help in getting primary union as the tissues cannot absorb this fluid and it is apt to turn to pus.

Case No. 5752.—Mrs. R., *aet.* 44, mother of two children, three miscarriages, has never been well since first miscarriage. During last six months has been suffering so much that she is now an invalid. Several who examined her thought she had a fibroid uterus impacted in the pelvis, but on opening the abdomen the tumor was found to be made up of two old pus tubes with the ovaries and uterus imbedded in them. The exact diagnosis was of little importance as the treatment was the same—namely, to remove the mass as soon as possible. The operation was very difficult and much blood was lost from the steady oozing from adhesions. She had to have an intravenous injection of artificial serum, besides a pint given by rectum during the operation. The round ligaments were sewed into the stump of the cervix to keep it from prolapsing and she made a good recovery.

Case No. 5771.—Mrs. L., a sempstress, *aet.* 38, appeared about 8 months pregnant owing to a large submucous fibroid which for three years had been causing profuse periods, and a great deal of pain. She had such a marked systolic murmur at the apex and such an irregular pulse that the anæsthetist was very much afraid to begin; but it improved under ether, and the large fibroid uterus was removed and the incision closed in 57 minutes. She made an excellent recovery and I can promise that her murmur will be gone completely in less than a year. Twenty years ago we should have been afraid to operate on such a case.

Case No. 5794.—Mrs. B., *aet.* 50, sent to us by Dr. Lesage of St. Lambert for profuse hemorrhages every two weeks for the last two years. She was the mother of 8 children and had been regular every month until the age of 48. She was curetted and the scrapings were submitted to our pathologist, Dr. Nichol, who reported that there was some heaping up of the lining cells of the tubules which

were enlarged, dilated, and tortuous, and he strongly suspected cancer. This suspicion was quite enough to justify me in urging hysterectomy, which was done on June 23, in this case the cervix being removed with the uterus and appendages. During the next few months she rapidly regained strength and weight, working in her garden every day. She has been seen by me quite recently and looks the picture of health.

Case No. 5818.—Mrs. G. W., *aet.* 31, mother of two children, one removed forcibly for vomiting of pregnancy, being two months pregnant was sent in for operation. As these cases generally have, she had a history of endometritis for many years. She had dysmenorrhœa so badly that she had to stay in bed for three days every month. She has now been vomiting constantly for three weeks. As I have had marked success during the last thirty years with alkali treatment, I put her on teaspoonful doses of *mistura rhei* and *sodæ*. At first she vomited most of it, but a few drops remained down, and in a few days she was retaining tablespoonful doses each containing fifteen grains of alkali. At first we kept her on milk and limewater, but by two weeks she was taking the regular hospital diet and went home. I am surprised that this simple treatment is not better known. I have found all the other drugs, such as oxalate of cerium and subgallate of bismuth, absolutely worthless, while *mistura rhei et sodæ* has not failed in more than 2 or 3 per cent. to cure completely the distressing and even dangerous condition.

Case No. 5837.—Mrs. C., *aet.* 33, mother of nine children, six miscarriages, was sent by Dr. England. She was a wreck from the miscarriages and suffered a great deal at her periods. I had removed her left ovary and done ventrofixation three years ago but foolishly listened to the entreaties of my colleagues to save one ovary, with the result that she continued to suffer just the same and both she and her husband were very dissatisfied. Here she was again with a heavy retroverted uterus due to a lacerated cervix and perineum, the ventrofixation of three years ago having failed. She would not consent to the removal of the right ovary so I did dilatation and curetting, removed the cervix, repaired the perineum, and shortened the round ligaments. She made a good recovery from these five operations, but it remains to be seen whether her pain will return or not.

Case No. 5856.—Mrs. W., *aet.* 26, was a very anxious one for Dr. Spier who sent her in June 12 with a temperature of 105 and a pulse of 118. She was the mother of three children, the last one three weeks old. Without any reason that we could find she developed a pelvic peritonitis. I am loth to curette these puerperal fever cases because so many die after curetting; while nearly every one of them recovers under washing and draining the uterus. Neither is it a good time to open the abdomen unless we suspect appendicitis. She improved very much under quinine and strychnine and hot douches, so that at the end of eighteen days, on June 30, I ventured to pass a dull curette over the fundus, bringing away some small pieces of placenta which had no bad smell. The uterus was then washed out and packed as usual. She made a slow recovery, but is now quite well.

Case No. 5877.—Mrs. S., was admitted on June 18 for bleeding since a miscarriage at three months which took place a month before. After three days of preparation we curetted her very gently and packed with iodoform gauze. Her temperature came down from 104° to 99° and she went home on June 30.

Case No. 5885.—Mrs. B., *aet.* 54, mother of 14 children, 3 miscarriages, was an interesting one because she had a cystocele and rectocele, with a lacerated cervix and perineum, which I treated by doing a vaginal fixation. I have been doing this operation frequently during the last year and so far the results seem to be much better than by any other method. I dilate, curette, and amputate the cervix, then open the anterior vaginal wall by a straight cut from cervix to urethra. The vagina is dissected off the cervix and bladder and then the bladder is separated from the uterus until it is possible to push the bladder high up and bring the uterus forward where the bladder was before. Two or three silkworm-gut stitches are passed through the vagina on the woman's left, then through the anterior wall of the uterus and out through the right flap of the vagina. When these are tied the uterus is securely attached to the anterior vaginal wall and it is no longer possible for the bladder to fall. Then the perineum is repaired so as to prevent the uterus or rectum from coming out through the vulva. These patients can get up in ten days and are not nearly so sick as those who have the abdomen opened from above.

Case No. 5888.—Mrs. S., 28 years old, mother of three children,

six miscarriages due to a retroverted uterus, for which I performed Alexander's operation.

Case No. 5909.—Mrs. H., 32 years old, never pregnant but suffers constantly from headaches and constipation, all three conditions due to retroversion for which I did Alexander's operation.

Case No. 5911.—Mrs. W., *aet.* 50, mother of four children, one miscarriage; last child 22 years ago. Menopause at 45. For the last three months has been complaining of severe pain down right side and obstinate constipation, due to a firmly fixed retroverted uterus. The ovaries, tubes, and appendix were dug out of a bed of dense adhesions and the uterus was freed and brought up and attached to the abdominal wall. Her pulse never went above 78 and she made a quick recovery.

Case No. 5814.—Miss P., came with a double inguinal hernia. I open the sac to make sure that it is empty, tie and cut it off, but leave the two ends of the ligature long enough to thread each into a separate needle which is passed into the abdomen about an inch higher up than the canal. These two needles are brought out about half an inch apart and the ligature tied on the external oblique. If the intestine tries to come out again and follows the sac it will only push against the strong abdominal wall high up above the canal.

Case No. 5933.—Mrs. R., mother of four children, was sent in after a miscarriage at four months. Although the uterus was rather boggy I carefully curetted and applied iodine; then did an Emmet on the cervix and put in a strip of gauze, after which she made a speedy recovery.

Case No. 5963.—Mrs. B., mother of six children, three miscarriages, complaining of great pain in the back due to a large retroverted uterus. It was replaced and a pessary put in to take the weight off the ligaments before doing an Alexander operation next day. The pessary was removed in a month. Good result.

Case No. 5968.—Mrs. M., *aet.* 21, been an invalid since she fell on the ice eighteen months ago striking the end of her spine and having a miscarriage. She had a retroverted but movable uterus and a painful coccyx which she could not bear to have touched. Every time she got up or sat down or moved her bowels or emptied her bladder or had intercourse she suffered extreme pain. Removed coccyx and did Alexander operation with complete relief to her symptoms.

Case No. 6036.—Mrs. —, 57 years old, menopause at 52, was quite pleased to have menstruation return four months ago. Examination showed pelvis filled with cancer. Cured away a large quantity of dead material and applied pure carbolic and then alcohol. Next day when she said "I suppose it is nothing serious;" I told her the truth—that she was beyond all hope.

Case No. 6059.—Mrs. M., *aet.* 52, ventral hernia; repaired by Mayo's method of sewing it up transversely instead of vertically and making the lower flap overlap the upper one so as to make a valve-like closure.

Case No. 6070.—Mrs. G., *aet.* 34, married ten years, never pregnant before, was treated for appendicitis in another hospital for three weeks but growing steadily worse was sent to the Western. Diagnosis of ruptured tubal pregnancy confirmed when abdomen was opened and found full of clots. Right ovary and tube and appendix were removed and she went home feeling well in twenty-one days.

Case No. 6084.—Mrs. M., *aet.* 42, abdominal hysterectomy for a fibroid the size of an orange, highest temperature 99°, highest pulse 96°. Went home in three weeks.

Case No. 6127.—Miss B., 22 years old, began to menstruate at 12 and has hardly ever been free from pain since. Been taking morphine for last two years. Removed both tubes and ovaries and appendix and she made a good recovery; no morphine since.

Case No. 6131.—Mrs. A., mother of three children, last one three months ago, ill in bed ever since with puerperal fever due to pus tubes and large inflamed appendix which were all removed with the ovaries. As the pus could be seen right through the wall of the uterus the tubes were dug out of the cornua and the holes in the uterus closed. She went home in 23 days.

The next six cases were removal of both tubes and ovaries and the appendix; one of them had the uterus removed as well, and another had ventrofixation. In all the hysterectomies I sew the round ligaments into the stump so as to prevent it from falling later. As I said before, no operative cases died during the six months, although on some days we did as many as five cases, which only shows how great the progress has been in Gynæcology and Abdominal Surgery during twenty-five years.

THE HYGIENE OF MENSTRUATION

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MENSTRUATION, characterizing as it does the beginning of sexual maturity, and pointing out by its absence the end of this period, attracted the attention of the older writers on medicine, but they concerned themselves only with its derangements and paid little or no heed to the hygienic measures by which some of these disturbances are to be avoided. The same practice has continued to the present day, and we find many pages upon the treatment of amenorrhœa, dysmenorrhœa, and menorrhagia, but little or nothing upon the hygiene of menstruation. Keeping close to the subject, it is perhaps true that there is little to be said, but that little is important and if well understood and respected would save many women from the serious discomforts which arise as the result of imprudence during the monthly sickness.

In the first place—what is menstruation? This is a term applied to a bloody discharge from the uterus which occurs at stated intervals, during sexual life. The time of its commencement, its duration, the amount and length of flow, the time elapsing between the periods, vary in different individuals, and certain of these characteristics are affected by race, climate, station in life, and the health of the individual. It is also true that external stimuli of various kinds appear to have a marked influence both upon its advent and its course. We must also admit that our knowledge concerning this vital phenomenon is incomplete in many directions.

As menstruation occurs only in man and some of the higher apes, physiological experimentation on lower animals offers little or no opportunity to solve various problems in this connection, and its cause is still a matter of speculation. Even the actual changes which take place in the uterus at this time are not yet fully agreed

upon by the various writers who have busied themselves in this line of investigation.

If we accept the views of Veit, there is, in the uterus: (1) A stage of premenstrual congestion with distended capillaries; an exudation of blood into the intercellular tissues, which forces them apart; and the formation of small sub-epithelial hæmatomata. (2) A discharge of this blood from the spaces between the epithelial cells, which are forced apart, and also from small areas where the mucous membrane is destroyed by the pressure of the extravasated blood. (3) A process of involution, in which the extravasated blood which remains is absorbed, the mucous membrane shrinks, and any small losses are repaired. In addition to the uterine changes, all the pelvic organs are engorged during the congestive period and the uterus enlarges and becomes softened, as well as the vagina and contiguous parts. In many women the breasts become full and tender.

Allowing that the observations of Veit are in the main correct, there is a need of such care during the menstrual period, even though physiological, as would be accorded were such conditions existent in other parts of the body. It has also been recognized for centuries that the nervous system at this time is unstable, that there is a feeling of malaise and often of abdominal fulness and discomfort at its beginning, and that a disturbance of the menstrual function leads to derangements of other physiological functions of the individual. Even the ancient Egyptian and Hindu writings show that the far-reaching effects of abnormal menstruation were appreciated and far from unknown. Theoretically, menstruation as a physiological function should need no therapy—practically, its hygiene is most important, for even among the aboriginal races, women are not exempt from the results of indiscretions at this time. While conditions of life have radically changed since early days, and the complex civilization of our time offers greater opportunities for the female in every direction; it has at the same time raised the requirements and heightened competition for those dependent, and increased the social obligations of those women not dependent upon their own endeavors for support. With the attempt of the female to enter into competition with the male in various employments the proper care at the time of the menstrual

period becomes a serious consideration, and it is probable that such lack of care is a drain upon the health of many individuals.

In view of these facts, every young woman should enter upon this important period of her life in the best physical condition, and the preparation for this event should begin from the earliest years. A too great mental effort, at the expense of bodily development, seems to be at the bottom of many menstrual troubles in New England; and in girls of delicate constitution study should give way to exercise in the open air and the development of a healthy body, even though at the expense of mental attainments.

As a result of the desire for education and competition in scholarship, frequently fostered by teachers and parents, young girls are often led to such mental efforts that their nervous and general physical stamina is seriously impaired, and they enter upon this period of sexual possibility in a state of enfeebled resistance. In every case an active out-of-door life (more considered to-day than ever before) proper diet, early hours, and rational mental activities, help to a solution of the first problem—good health at the start. Furthermore, with a sound body will come that ability for self-control at this period of nervous instability, so lacking in our neurotic young women.

Before, if possible, but at least with the earliest menses, the young woman should be informed either by mother, physician, or a well-posted friend, as to the nature of this new function and the care to be exercised at the time of its occurrence. It is most unfortunate that children should be left to absorb such matters from playmates, and by chance—often without information from what may be termed legitimate sources. It may be also well said, that advice upon this subject is, in most instances, best left to the family physician; for it is evident that the hygiene of menstruation has not yet reached the stage which the popularization of medicine in other directions has attained in the daily press.

What general rules may be laid down for the guidance of the young woman? At the beginning of this function, rest during the first day or two is to be wished for at the least, and proper care in regard to food and evacuations of the bowels. Exertion of any kind is to be frowned upon, and if the flow is beyond what may normally be expected, rest in bed is to be recommended, and abso-

lute freedom from mental and physical strain. Some have gone so far as to forbid school during the period from 12 to 15 years, but it is not certain as to whether this is necessary, or even desirable. Even after the monthly flow is well established, dancing, social engagements, and athletic exercise should be avoided, as well as everything which in any way tends to overexertion or to excite sexual feeling, which is often heightened at this time.

One of the most common causes of disturbance of menstrual function is "taking cold." While many troubles are laid to this indiscretion, with which it has no possible connection, it is also true that dysmenorrhœa, vaginal discharge, menstrual suppression, and endometritis may arise after carelessness in regard to bodily protection at this time. Wet feet, cold seats, chilling of the body, affect the distribution of the circulation and lead undoubtedly to inflammatory processes in the virgin genital tract. It is also well recognized that the same causes may lead to the recrudescence of old processes—infectious and otherwise.

There is much misunderstanding about the subject of bodily cleanliness. At no time is care of the genitalia more to be desired, and washing of these parts several times daily with warm water removes the dried blood and prevents irritation. The vaginal douche should not be used by unmarried women at the close of the menstrual period. Clothing which has been soiled should be laid aside and napkins renewed often enough to prevent excoriation from the dried discharges. In warm weather, or under proper conditions, no harm can come from a warm bath taken before retiring; but it is especially to be observed that under no circumstances should the woman enter a cold bed following such ablutions, or allow the body surface to become chilled. These, in the main, are the points to be observed and though it is impossible to provide exact rules for all the exigencies of every-day life, if the general principles are borne in mind, there will be less irregularity in menstruation, less dysmenorrhœa, and more women who pass through active sexual life with no dread of the monthly sickness.

Pædiatrics

EYE-STRAIN AMONG SCHOOL CHILDREN

BY AARON BRAV, M.D.

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WHEN we consider the fact that there are fully twenty million school children attending the various schools of our country and that correct sight, that is normal vision with ease, without any special effort or reinforcement of the stored nervous energy, is essential to the absorption of presented instruction, the necessity of detecting and correcting any existing error of refraction becomes self-evident. Children are very often considered stupid by their parents when they fail to keep up with the outlined studies, when as a matter of fact they do possess the native intelligence to grasp and absorb and retain the instruction given, but are greatly hampered by visual defects resulting from some existing error of refraction or muscular imbalance that is amenable to treatment. Very often has it been demonstrated to the satisfaction of all concerned that an apparently stupid child who has been delinquent in his studies has been transformed into a diligent, normal student through the correction of an error of refraction by means of well adjusted glasses which have relieved the eye-strain, allowing the child to use its otherwise consumed nerve energy for the absorption and retention of the subject-matter presented by the teacher. Eye-strain is an important factor in the life of a child during the school term. It should be remembered that the school period marks an important epoch in the evolution of the child. The nervous system during this period is not yet fully developed, is as yet unstable, while the atmosphere of school life adds a heavy tax upon the general vitality of the child, and every physical defect only adds to the discomfort of the child and interferes with its normal intel-

lectual advancement. It is indeed a conservative estimate to state that 40 per cent. of the school children suffer from eye-strain in one form or another.

Eye-strain may manifest itself in different ways. The symptoms may sometimes be purely local. In such cases the little patients may complain that they cannot see well at the black-board. Occasionally they can see what the teacher writes on the board but they mistake some letters. A non-observant teacher under such circumstances may mistake the visual deficiency for actual mental delinquency and consequently give the child a bad mark, which in reality it does not deserve. The school authorities indeed should have an experienced ophthalmologist to detect these latent errors of refraction for the benefit of the children. The ordinary young medical inspector is often not able to judge these unfortunate little ones, who though diligent and industrious cannot keep pace with the other children without special effort which only tends to aggravate the condition and give rise to more serious symptoms of a reflex character. In the cases where the asthenopia manifests itself in local symptoms the child is unable to do its home lessons which in the majority of cases have to be done under bad illumination. The letters blur. The child will then say that after a few minutes' reading the reading matter all runs together or the letters appear to dance. The little patient often tries to wipe away the disturbing factor by rubbing its eyes. Closing the eyes for a little while gives some relief, which enables the little searcher in the field of rudimentary knowledge to continue with its previous work for a few minutes longer, only to be confronted again with the same difficulty which compels the child to discontinue its work. It is indeed a pity to observe these children struggling against a physical defect that could easily be remedied. The blurring of the reading matter is usually caused by an overlapping of the images resulting from a disturbed relation between the muscles of accommodation and the muscles of convergence. Occasionally the local symptoms manifest themselves in a twitching of the lid or twitching of some of the adjacent facial muscles. There may be no pain in the eyeball. Often the local symptoms do not manifest themselves in visual disturbances. The visual act may under re-enforcement be normal but as a result of the eye-strain the lids may become

congested and red, the margins of the lid may be scaly, giving rise to a blepharitis, and less often styes develop. This is simply nature's method of calling our attention to an existing defective visual apparatus that is doing overwork which will eventually produce more serious reflex disturbances. These reflex symptoms may either accompany the local disturbance or they may be present without any local manifestation of eye-strain. The fact therefore that the child does not complain of pain in the eyeball or of visual difficulties, or the fact that no other local symptoms, such as congestion of the lids, styes, twitching of the eyelids, are present is not sufficient evidence of a normal visual apparatus, and the eye as the cause of an existing reflex disturbance even in the absence of local symptoms cannot be excluded with any degree of certainty. The only way to exclude the eye as the offending organ which may be responsible for the reflex symptoms that make school life a burden instead of a pleasure is by a careful detection and correction of any error of refraction and muscular imbalance. Muscular disturbances interfering with the power of convergence even in the mild form where one of the internal recti muscles fails to converge to fix the near object have the same baneful effect. However in school children practically all convergence insufficiencies are secondary to an existing error of refraction that can easily be corrected by carefully prescribed lenses. In a physical race we would not place a lame boy with one that has normal limbs and expect him to do as well as his playmate, yet this is precisely what is expected of the boy whose muscles are not well balanced. He is to keep pace in an intellectual race with the rest of the children whose ocular muscles are well balanced and of course he must fail. Twitching of the eyelids is often a symptom of eye-strain and when accompanied by twitching of some of the other facial muscles the condition is often diagnosed as chorea and treated with arsenic when as a matter of fact some astigmatism as a rule is its real cause. I do not wish to be understood as claiming that errors of refraction are the cause of chorea. It is my firm belief that neither epilepsy nor true migraine nor true chorea are caused by eye-strain, Dr. Gould to the contrary notwithstanding. These choreic twitchings are not true chorea, but reflex irritation resulting from eye-strain.

The reflex symptoms may also vary in different children and in some cases, as we shall see, a vicious circle may be established which gives rise to serious disturbances and makes the life of our little patient miserable indeed. School life under normal conditions should be a pleasure rather than a burden to children. Whenever school life ceases to be a pleasure to the child a careful examination will reveal some physical defect that interferes with the child's normal development. Among these physical defects eye-strain is one of the most frequent to give rise to various reflex symptoms.

Among the many reflex symptoms resulting from eye-strain is headache. From the ophthalmologic point of view this symptom is of as much importance as the local direct ocular symptoms. Usually, however, when the local symptoms are present relief is much sooner sought for by parents who can recognize the visual defect because of the complaint of the child which has direct reference to the visual organ. Parents often cannot and will not be convinced of the relationship existing between headaches and eye-strain and consequently will not seek relief through glasses to which they are usually opposed. This opposition to a child wearing glasses during school life is to be found not only among the ignorant classes but also among the better, intelligent classes. There seems to be a universal idiosyncrasy to this rather important therapeutic measure in the domain of pædiatrics.

The headaches in consequence of eye-strain may be localized. Most frequently they are frontal, or temporal radiating to the frontal region, less frequently occipital, and occasionally they are diffused in character. Sometimes the pain is limited to the eyebrows around the superciliary ridge, when it is mistaken for supra-orbital neuralgia. The headache may be the only symptom of eye-strain in the beginning; when however the child is compelled to struggle with its visual deficiency other symptoms of a reflex nature accompany the headache. Frowning is of course a pathognomonic sign in children. The corrugator supercilii muscles are always called into play when errors of refraction of the astigmatic type are present. Half closing the lids so as to narrow the palpebral fissure in order to exclude some rays of light is another pathognomonic sign of astigmatism. Usually these two signs manifest themselves simultaneously.

Headaches due to eye-strain usually come on after using the eyes for close work. They may be constant, and, paradoxical as this may seem, they may appear in the morning after a night's rest. The fact that the headache comes after a night's rest should not lead us to exclude eye-strain as a probable cause. It is our experience that often these morning headaches are caused by eye-strain, especially where there exists some disturbance in the equilibrium of the extra-ocular muscles. As a result of these persistent headaches the child feels irritable and indisposed; it does not indulge in the usual frolics so natural to children during school life. Frequently the headache is accompanied by dizziness. Occasionally this dizziness reaches a considerable degree, so much so that things seem to turn about in the school room; the child closes its eyes and rests its head on the desk so as to get relief. After a little rest the dizziness disappears and the child feels relieved, but in reality after such attack it is not fit for school work that day. The child however usually continues its lessons only to its own detriment. When again in the open air the child feels better and so no one is consulted in the matter and no one thinks of the eye as the possible offending organ that is responsible for the reflex symptoms. In consequence of the eye-strain and its resulting headache the child loses its appetite and may occasionally even have attacks of vomiting; especially is this possible when there is astigmatism with oblique axes and some muscular imbalance, and particularly so in nervous children. In these cases there develops a gastro-intestinal disturbance. The child cannot enjoy its meals, eats very little, and rather often goes to school without breakfast. The resulting weakness from lack of nourishment thus obtained only tends to aggravate the asthenopia and the child feels still more miserable. Soon it loses color and looks pale and anæmic from both lack of nourishment and the continuous strain and drain upon the yet unstable nervous system. The child becomes weakened and as the weakness increases the asthenopia becomes more marked, which in turn has a still more deleterious influence upon the child's general system, and so a vicious circle is established that eventually breaks down the child's constitution. The child is often treated for its gastro-intestinal disturbance, or for anæmia, or occasionally for some nervousness. This treatment

is of course essential and may give the child some relief, but it is evident that unless the cause is removed the patient will not be cured. Keeping the child out of school for a little time is of course a rational therapeutic measure, but the evil results of eye-strain will soon manifest themselves again as soon as the child returns to school and resumes its work. Glasses alone can remove the cause of the little innocent's sufferings and we should not withhold them on cosmetic grounds. The evil results of eye-strain are so well known to the ophthalmologist that it seems strange indeed that the general public, and occasionally the physician, should neglect it. The school authorities should look into the matter of ocular examination and an ophthalmologist should have charge of the examination—such examination should be made twice: during the beginning of the session, and in the midwinter vacation.

There is a tendency among medical men to think that the child is overworked in school. I have no sympathy with these men. I am fully convinced, after careful study, that the time the child spends in school, which is four and a half hours daily, is not too much, especially when we think of the fact that there are recesses during this time. The morning hours are from 9 to 12, with twenty minutes' pause; about ten minutes is consumed by arranging classes and songs, which act as a stimulant and source of enjoyment for the child. The afternoon hours are from 1.30 to 3 P.M. This includes twenty minutes' physical exercise. A normal child should have no difficulty in getting along well during these hours. It is only the physically defective that feel the strain. Many children are of course hampered by constitutional weakness but many are handicapped merely because of eye-strain. Whenever a child does not keep pace with his studies, when he suffers from headaches, is irritable, is pale, has dizzy spells, or even when he is ill-disposed,—not taking part in the usual childish plays with his fellows,—the eyes should always be examined. Not that all troubles are caused by the eyes but a great many can be avoided by a careful correction of errors of refraction which are responsible for many of the reflex symptoms as a result of eye-strain.

It is needless, I am sure, to emphasize to this body that such errors of refraction must be corrected while the child is under the

influence of a cycloplegic. It is absolutely impossible to correct existing errors of refraction in children without a mydriatic. In this connection it will probably not be amiss to mention the deplorable fact that the advertising optician has still a great hold on the public and that many parents take their children to him for glasses. The opticians have of late taken advantage of the indifference of the medical profession in jealously guarding the title of doctor for which they had to give years of study, and in the absence of any laws regulating the practice of this ophthalmic branch of medicine, they assume the title of doctor and ply their trade publicly, and this with the common passive consent of the county, state, and ophthalmologic societies. They are no longer to be found only in the stores selling glasses under the name optician, but ply their trade in private offices with regular office hours under the assumed title of doctor and eye specialist, and of course the unsophisticated public cannot differentiate them from the regular ophthalmologist. To them the sign, doctor, is sufficient evidence—as indeed it should be—of a regular college diploma and state license. Thus the people are easily misled and the progress of ophthalmic therapeutics is retarded. The profession is largely responsible for this condition of affairs. As a matter of fact, there are even to-day medical men who do not think refraction to be a branch of medicine. The remedy is in the hand of the medical profession and the county medical society should try to remedy the evil as far as possible. The county medical society should instruct its legal representative to inquire whether or not these opticians could be prevented from using the title doctor which they did not obtain from chartered medical schools. We do not seek any class legislation, but we wish to prohibit the abuse of the title doctor which some people use as a cover to defraud the public. It seems that in our endeavor to lead an ethical life we fail to protect ourselves against the charlatan and quack using the honorable title doctor for selfish purposes.

Credit is indeed due to the school authorities who, in notifying parents of any existing ocular trouble in their children, distinctly advise them to consult an oculist and not an optician. School children are subject to various reflex symptoms resulting from eye-strain, but it is sometimes difficult, even for the medical in-

spector, to convince parents of the relationship of headaches and eye-strain, for they cannot see any abnormality in their child's eye. They may notice when the child is myopic but are not capable of judging a latent hyperopic or astigmatic condition. As a matter of fact, however, most children suffering from eye-strain are not of the myopic type, but rather of the hyperopic, simple, compound, or mixed astigmatic type. To these children school life becomes a heavy burden, for they struggle with a physical abnormality that retards their progress and often the physical unbalance manifests itself in mental deficiency. All children suffering from headaches, dizziness, irritability, poor appetite, and nervousness should be carefully refracted and any error of refraction carefully adjusted by an ophthalmologist, for in many cases we find that the underlying causal factor in these little patients is eye-strain.

Neurology

TABES DORSALIS—ITS RATIONAL TREATMENT IN THE LIGHT OF ITS REAL PATHOGENESIS *

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BEFORE considering the treatment of tabes dorsalis it is necessary to have a clear notion of its pathogenesis, so that one may always keep in mind the process against which efforts are to be directed. The review I shall attempt is all the more required in that there will emerge from it conclusions entirely at variance with the pessimism of the dystrophic theory so recently re-emphasized by Ferrier and still later by Mott. Both of these writers have, as I hope to show, dismissed too cavalierly the considerations regarding the posterior roots which Nageotte was the first to place forward convincingly. An examination of his facts should convince the impartial that tabes cannot be a dystrophy of the sensory protoneurone; for it is a degeneration secondary to a meningitis of specific nature which falls most heavily upon the posterior roots from anatomical and physiological causes.

In serial sections of the roots of the spinal cord one cannot fail to see that the meninges, in approximating to and ensheathing the radicular nerves, leave a potential space, a canal, for a considerable distance along the roots where the anterior joins the posterior.

Nageotte's serial sections of the roots clearly show that just at this canal occurs a round-cell infiltration of the perineurium and epi- and endoneural sheaths. This spot is, in the lower lumbar and sacral nerves, a long way from the pial ring which Redlich and Obersteiner, and following them Orr and Rows, believe to

* Read in the Medical Section of the British Medical Association held at Belfast, July 30, 1909.

mark the commencement of the posterior column denegeration. The inflammatory process upon the radicular nerve differs only in intensity, but not in nature, from that upon the meninges generally speaking. But on some spots there may even be found a well-marked granuloma of minute size and this may sometimes be seen in the process of degeneration into a cyst.

This exudate, which not only lies upon but infiltrates the endoneural trabeculæ of the roots, cannot but impinge upon and injure the nerve fibrils. And it is their destruction at this spot which induces the degeneration of the posterior columns of the cord. But it is not only the intramedullary fibres which atrophy but those in the roots as well, that is, in their course from the site of the lesion towards the cord. The results do not differ from those caused by the root-pressure of tumors of the theca vertebralis or by tubercle of the same; the effects of the increased intrathecal pressure caused by cerebral tumors are also similar. In this latter example, however, the lesion of the root is produced mechanically by the pressure forcing apart and flattening the nerves fibres. But the site of the process is the afore-mentioned canal called by Nageotte the radicular zone.

In the root itself, however, regeneration is possible when the lesion is absorbed, if that takes place. But within the cord no regeneration can occur; for no neurilemma is possessed by the fibres there.

Now, as a granulomatous process often undergoes resolution with only an inconsiderable cicatrix, many of the roots in tabes may not appear degenerated to the naked eye on account of the new-formed fibres maintaining their bulk and normal circumference. But under the microscope, such a nerve shows an abundance of new-formed fibres, many of them ending in the small, curling neuromata so familiar in amputation stumps. These regenerating fibres, however, cease at Redlich's ring. Of course, when an extensive fibrosis has occurred the fibres regenerating from the ganglia cannot traverse the radicular zone; and we find then the flattened and empty roots which so often occur in cases of long duration.

In some individuals, the adherence of the meninges may be more areolar and extend nearer to the ganglion; and this peculiarity may account for the few cases in which a diseased condition has been

found in these organs. But of course, one must carefully distinguish from this the chromolytic "reaction at a distance" which occurs in every nerve cell whose axon is injured.

It may be contended that neither spinal tumors nor Pott's disease without deformity produces tabetic symptoms; but it must be remembered that spinal tumor affects only a few roots, does so massively, and gives rise to numerous cord symptoms which preponderate; while some of Alquier's cases show that a tuberculous process can indeed for a time simulate that of tabes. In cerebral tumors again, tabetic symptoms may often be found when searched for clinically; although of course they are only *fruste* and are quite overshadowed by the cerebral disorder.

To these views, it has been objected that meningitis is more often absent than present in tabes. But this can be said only of macroscopic lesions. Careful search with the microscope always reveals meningeal exudates, and the fibrous sequelæ of many more. It is these that Ferrier in championing the dystrophic theory has mis-called "thickenings secondary to nerve degeneration." But an unprejudiced study of various meningeal localities in the same patient clearly shows their inflammatory nature. Moreover, the lymphocytosis during life indicates the meningeal irritation responsible for the round cell infiltration and exudates.

It must not be forgotten that lymphocytosis is found in 40 per cent. of luetic cases during the eruptive stage, and that it is often accompanied by a sluggish reaction of the pupil to light. It indicates an eruption, so to speak, in the meninges; and like all such secondary phenomena tends to undergo resolution spontaneously or under treatment.

Moreover, it is not rare for other meningitides to cause secondary intraspinal degeneration through implication of the posterior roots; for the researches of Alquier regarding tuberculous pachymeningitis, as well as Lejonne's studies of cerebral tumors, show the frequency of such intraspinal secondary degeneration.

That tabetic lesions tend to be segmental is surely not against their radicular origin; for recent researches have refuted the notions of Brissaud and Head that intraspinal segmentation differs from that subserved by the roots, at least where the sensibility is concerned.

Ferrier's other objection that well-marked intramedullary degeneration may occur in the absence of inflammation or atrophy of posterior roots is answered by the previous considerations as to the regenerative power of these, and in addition by the experiments of Bickles, who found that the roots completely regenerated after section, leaving their corresponding intraspinal path sclerosed just as in tabes.

The escape of the anterior roots, which he brings as a further objection, is merely relative and functional, because of their rapid and effective regeneration; besides which their course within the meninges is shorter than that of the posterior roots. It is very significant that the parts affected by tabes are just those of which the radicular nerves and roots have the longest course, that is, where they are the most exposed to any cause which irritates the meninges. They are shortest in the cervical and upper dorsal regions, where symptoms are rarest; they are longest in the lower lumbar and sacral regions, where the symptoms are commonest and most often commence. Moreover, the frequency of cranial-nerve symptoms is explained by the prolonged exposure of these to meningeal irritation during their passage across the subarachnoid space. And moreover, the implication of the optic nerve in this situation, where it is no longer a posterior root but a body of relay neurons, is another proof that the process is not a specific, protoneuronic dystrophy. Again, most persons lie rather on the back than the face; and this may partly account for the lesser implication of anterior roots. The lessons of hypostatic pneumonia, and of abscess draining, surely indicate the importance of posture.

Marinesco and Minéa have also minutely studied the radicular nerves of tabetics, and have shown definite regenerating fibres. The processes of regeneration are most conspicuous in the early stages; they are not only in the roots but extend to the ganglia, and there is a great difference between the internal and external poles of these, the persistence of old axons being much greater at the latter. The fibres are embryonal and resemble those found in regenerating nerves. They usually arise from the glomerulus, and are generally collaterals, though they may be rejuvenations of old nerve fibres, appearing as a fine black-staining fibre from the extremity of an axon which has become conical; they are hard to trace. They finish

in a mass of variable forms, and occur mainly at the emergence of the radicular nerve at the superior pole. Marinesco considers them as a reaction of the cytoplasm caused by direct irritation; for they occur also in transplanted ganglia and in myelitis. They, therefore, believe that the tabetic degeneration is a primitive atrophy of the central branch of the spinal ganglion caused by syphilitic toxin; for they cannot otherwise explain the fact that changes occur not only in the radicular nerve, but also in the intra-ganglionic fibres. They, therefore, believe that the interstitial and vascular inflammation is only concomitant and secondary.

Against this view must be urged the vast disproportion of the degeneration distal and proximal to the radicular zone respectively. It must be remembered that many observers have found the ganglion cells implicated; and the explanation of this is simply the extension backwards of the process which has begun at the radicular zone, for this is always much more gravely attacked. It is possible in this way to explain the peripheral neuritis in certain cases. And indeed, in a later communication, the same authors point out the inverse ratio between the number of uniform fibres and those degenerated, both within the ganglion and in the radicular nerve. The regenerating fibres in the more chronic cases rarely reach the posterior roots proper. They traverse a most circuitous route, often turning backwards. The degenerations extend right back to the ganglion; and the axolysis and interfibrillary accumulations resemble those in sectioned nerves; but the process differs from this in that a degeneration extends back to the ganglion, which does not occur after a mere section. Moreover, the regenerating fibres remain embryonic, all of which goes to prove the primitive intoxication preventing them from complete development.

These conditions entirely negative a dystrophic explanation of a process where anatomical regeneration is so conspicuous a factor, even though from mechanical and perhaps chemical and biological reasons, the regeneration may not become functionally effective. Moreover, it is inexplicable that a dystrophy should be confined to one process of a cell only.

The early meningeal infection, the continuance of which eventually produces tabes dorsalis, is illustrated by a patient of Gaucher and Maloizel, who was entirely refractory to mercury, and who

seven times presented exacerbations of cutaneous lesions accompanied by meningeal syndromes of fever, headache, vomiting, stiffness of the neck, and lymphocytosis.

The mode of penetration of the inflammatory process into the optic nerve is illustrated by Babinsky and Chaillous's study of the visual fields in tabetics. They show that there is no particular type, but in most cases an irregular contraction for white, usually on a par with the generally enfeebled acuity of vision, though in a few cases visual acuity is good. True central scotoma is rare, and is generally due to an added intoxication by tobacco and alcohol; but central vision may be abolished consecutively to that of a sector of the field, and may even leave part of the peripheral field intact. But Galezowski has shown the central vision may be lost very rapidly as soon as a half sector of the field has been implicated, and that this is due to the situation of the central fibres in the heart of the optic nerve and tract, to reach which meningeal inflammation requires considerable time.

Lesions of the sympathetic fibres are quite common in tabes, the lesions occurring as they pass from the gray matter of the cord, probably Bruce's intermediolateral column, to the sympathetic chain, *via* the spinal roots. Such lesions may even be focalized, as in the case of Jeanselme and Sézary, in which a left-sided cervical sympathetic syndrome along with hemi-hyperæsthesia of the face and head occurred without fever or other general symptoms, but with marked redness and herpes of the throat, ear and face, with a myosis and reflex iridoplegia. The man had always been subject to hepatic attacks, but not of this character; there were extensive hyperæsthesia, loss of tendon reflexes, lancinating pains since a year before, and staggering gait. Lumbar puncture showed lymphocytosis. The sympathetic symptoms largely cleared up in a few days under mercury.

Muscular atrophy in tabes is being more and more frequently reported. Thus Camp reported to the Philadelphia Neurological Society two cases of tabes which began with a muscular palsy of the extensors of the foot; he emphasized the relationship of this to ocular palsies. Lapinski too published many cases beginning with motor paralysis; but he believes them due to loss of tonus by lesion of the posterior roots, not taking into account the researches

of Nageotte on the anterior roots. The evanescence of the paralysis which occurs in early tabes is illustrated by the cases shown by Crouzon and Nathan at the Paris Neurological Hospital. There was total bilateral ophthalmoplegia, masticatory paralysis, and unilateral facial palsy with hyperacusia, without sensory troubles of the face nor any part of the body; but he had lightning pains, numbness, loss of tendon reflexes, and slight troubles with the sphincters. No muscular atrophy followed and the paralyzes all disappeared except that of the right abducens.

This case may be compared to that shown by Lamy, in which, however, the muscles atrophied after $11\frac{1}{2}$ years of slow progress, the only other signs being reflex iridoplegia and loss of one knee-jerk; lightning pains had never been complained of.

Souques too reported a similar case of external ophthalmoplegia only, with palsy of the palate, respiratory crises, and rapid pulse. In the limbs the only symptoms were formication and occasional crises of pain; there were no sphincter troubles. There was the possibility of added infection in this case causing a poliomyelitis inferior.

Raymond's cases, again, of muscular atrophy of the arms are most striking, so is that of Souques, in which the muscular atrophy was of the Aran-Duchenne type, without sensory troubles in the arms, while in the lower limbs lightning pains had occurred, and the left knee and right Achilles reflexes were abolished although both great toes extended on stroking the sole, and there was reflex iridoplegia. He interprets the symptoms as all being due to the same cause, *viz.*, syphilitic meningomyelitis, and cites in support of this the thirty cases of progressive muscular atrophy in syphilitics collected by Leri, and the cases of Rendu and Laignel-Lavastine, in which Aran-Duchenne palsy recurred in the course of general paralysis. In all these patients except one who refused examination lymphocytosis was found.

Localized meningo-radiculitis is still more apparently the origin of muscular atrophy in a case of the author's. It is one of cerebrospinal lues whose symptoms are mainly mental, but which shows unilateral hyperæsthesia of L.V. and S.I. only, along with marked atrophy of the corresponding glutei.

The case of meningo-radiculitis reported by Marfan and

Oppert shows definite localization of sensory and motor troubles, —L., IV., V., and S.I., II., III., IV. being implicated. There was then, however, no iridoplegia, though the Achilles and patellar reflexes were absent.

Mott objects that the Argyll-Robertson pupil is too constant to be explained by the incidence of a syphilitic process. But it is not a case of random metastases as he assumes, but of general involvement of the meninges which determines a slowly progressive involvement of nerve fibres which are rotted by the diseased membrane in proportion to their long exposure, and inversely to thickness and covering in relation to the membrane. In this we should find a strong presumption that the photoreflex arc is particularly exposed to attack, whether because of superficiality of its course or a peculiarity hitherto unsurmised. It is to this rather than the invocation of metastases that we must refer its so frequent implications; as of course it escapes in merely focal syphilitic affections of the central nervous system, unless these too are complicated by a meningitis. As Nageotte long ago remarked, lymphocytosis greatly precedes iridoplegia. Even lost knee-jerks often do so as well.

Researches in this direction, following up those of Marina, might show that the reflex iridoplegia was a purely sympathetic phenomenon, and due to the implication of the slender and exposed non-medullated fibres during their course from the carotid plexus to the ciliary ganglion; for the photomotor reflex may be due entirely to inhibition of the ciliospinal centre ceasing to antagonize the tonus-regulating sphincter pupillæ under the control of the third nerve. It must be remembered that some tabetics' pupils are fixed in dilatation instead of in the more usual contraction. The Argyll-Robertson pupil might be regarded then as one not dilating to the absence of light, which presents the impression to the observer of not contracting to light; for of course it has no stimulus to do so unless in a state of dilatation out of proportion to the illumination it undergoes. This, however, is a mere surmise, and one subject to correction.

The fact that only from 3 to 5 per cent. of syphilitics should ultimately present symptoms of tabes or paresis is no more remarkable than the similarly small percentage which suffer from sclerosis or gumma of the liver, which no one pretends signifies a special

degenerative predisposition of the hepatic cells in these individuals; for it is clearly recognized that a gumma is a focal infective granuloma, while in diffuse sclerosis the atrophy of glandular cells is entirely secondary to the connective tissue inflammation. Why then should one desire to invoke as an explanation of tabo-paralysis such a tendency to parenchymatous dystrophy as is invoked by Mott, following Fournier. Such an explanation is completely negated by the constant and continuous growth of the axons from the cells of the posterior root ganglia in their attempts to traverse the inflammatory focus in the radicular zone. It is against all we know of pathology to suppose a dystrophic neuron to be capable of such persistent growth, whereas the real explanation is before one's eyes in the meningitic focus upon the radicular nerve.

Again, Mott, for reasons which he does not specify, rejects the view of Lesser, Bose, etc., that tabes, etc., are quaternary syphilis and comparable to the scleroses of orchitis, glossitis, etc., and that the degeneration of the noble elements is secondary to the meningeal and perivascular infiltration and to the proliferation of glia; but the facts I have presented make it difficult to reject these views.

To support the dystrophic theory, he is driven to contend for numerous hypotheses, such as that "the nerve cells of a syphilitic acquire a habit of increased metabolic activity continuous during life, and that this contributes to excess of lipoids in the blood. This tendency to decay increases, and is the cause of increased functional nervous activity in the early stages, and this is specially injurious with regard to the genetic function on account of the loss of the nuclein substances of the sperm because the lipoids *may be* products of nuclear activity, and the highly phosphorized nuclein *may be* really the source of vital action."

The excess of lipoids may as easily be explained by an increased breaking down of cells, not necessarily even those of the central nervous system, due to the chronic inflammatory process of specific kind. We are very far from being able to affirm a perverted habit of cytologic activity, and to base a doctrine upon so slender a hypothesis is to say the least premature. Moreover, we have no proof that loss of highly phosphorized nuclein of the sperms by sexual activity in any way injures the organism.

Such speculations strike the writer as being at variance with

the methods which science has learned to adopt in order to safeguard its postulates from the incursions of ill-founded theories.

Of course, such conclusions connote the uselessness of anti-syphilitic treatment to a system which has already "over-immunized itself against the syphilitic virus" and compel recourse merely to suppression of causes which use up nerve energy and overturn metabolic equilibrium.

Recent evidence tends to show that there is as much validity in administering mercury in tabes and even paresis when diagnosed early as there is reason to do so in arterial degeneration and gumma whether in the central nervous system or not. The latter are both unamenable to such remedies in so far as the contiguous parenchyma has been destroyed; and atheromatous arteries have no more power of regeneration than has the central nervous system. But no one withholds mercury for these reasons; for though it cannot restore dead tissues, we believe that it at least increases resolvent activity and aids in diminishing the gravity of the infective process. We are not yet certain whether mercury and iodides act antibacterially or as antitoxins directly, or whether they do so by stimulating the defensive reactions of the organism by means of the internal secretions or otherwise. There is even a possibility that just as digitalis may shorten the life of the individual by using up cardiac energy prematurely, so may mercury exhaust the defensive powers of the patient. Thus Kron concludes from the study of 482 cases that more treatment connotes earlier tabes, and Vraveri believes in low doses from his experience of earlier cases, many of which lacked Westphal's sign and had only one symptom.

Faure of Malou has pointed out that mercury, while it does harm to tabetics with chronic cystitis or intestinal troubles or cachexia, is of great benefit even in some cases of tuberculosis if not pulmonary. He quotes a case of a man of 40 who had had tuberculous ostitis and was attacked by severe tabes with multiple symptoms. After five years of mercurial treatment, he is in excellent health, and most of the annoying symptoms have disappeared. Moreover, in tuberculous cases not treated by mercury, relapses are very frequent.

In Donath's case the knee reflexes, which had disappeared five

months after the first symptoms showed themselves, returned twenty-two months later.

The experience of Erb and Babiniski strongly confirms the usefulness of mercury; they find that the pain, especially, disappears after thorough treatment, and that the progress of the disease ceases, although as before explained, regeneration cannot be expected. Lesser believes that the Wassermann reaction is of use in controlling the administration of mercury in that it becomes much feebler during treatment, and that he has found it in only 50 per cent. of tabetics on account of the well-known tendency to arrest in this disease, whereas complement is deviated in all cases of paresis.

It must be recollected that the specific meningitis which causes tabes is often complicated, especially in later life, by arteriosclerotic conditions. These long ago caused Gowers to place degenerated spinocerebellar tracts in the picture of tabes. In estimating the pathogenesis of tabetic disorders such anomalies must be taken into consideration. Thus Long reports a case of spastic tabes where the reflexes disappeared only at the end of the disease, and the roots were little altered.

In the early stages too the pial trabeculæ, in reacting to the noxa, may show periarterial infiltrations, as shown first, as Beutter and Schroeder found in five cases, not only in the posterior column, but in the whole circumference of the cord, optic nerve, and brain-stem as well, though not in the cortex. These appearances were not found in alcoholic pseudo-tabes. This is the process that occurs in the cortex of paralytics; but according to Alzheimer, it rarely occurs within the cord of tabetics, although he has always found, in common with Nageotte, infiltration and thickening of the pia mater itself, as has Spiller in most cases.

Another source of error is the acute and grave degeneration of medulla and nerve which sometimes occurs in syphilitics, whether tabetics or not. Thus Preobraschensky reported a case which died in 13 days after onset of an acute muscular atrophy of limbs and trunk. It was only at the end of the illness that pains and irregular pupils ensued; the man had had syphilis fifteen years before. Post mortem: atrophy of the anterior horns and infiltra-

tion of the vessels of the cord, with atrophy of the roots near the cord were found.

Crouzon and Villaret report that after some months of right sciatica (meningomyelitis) a man of forty-two died in eight days of an acutely ingravescent ascending paralysis. François-Dainville reports that seven years after infection with no symptoms or treatment, a woman of 23 was admitted, owing to albuminuria. She had no cerebral symptoms, not even headache; but she died in nine months, a tabetic. Post mortem there was found a meningovascularity like that first described by Déjerine and Sottas.

I have by no means exhausted either the facts or the arguments in favor of the point of view here presented; for they are accumulating daily; and while in Paris last month I myself observed an extraordinary number of cases of *tabes fruste*, local radiculitis and early cortical manifestations of luetic meningitis.

When seen and treated in this early state, these conditions may be at least arrested in a large proportion of cases. This is particularly the case with regard to the ocular symptoms, but mercury must be given here by intravenous injection so that it may rapidly gain access to any diseased focus. In Abadie's clinic during the last eight years an average of thirty cases have been injected per day; and there has never been the least accident, phlebitis or pain never having occurred. In St. Louis, on the other hand, these complications are not infrequent, and they are due to timidity in making the injections and to ones' not adopting the safeguard of drawing a little blood from the vein into the syringe before injecting the solution. Wm. Froguer informs me that a considerable number of cases of tabetic optic atrophy have in this way apparently been arrested, sometimes with considerable recovery of vision. Not only so, but the lightning pains from which many patients have suffered for years (although they do not come to the ophthalmological clinic for these), have often been treated without avail as rheumatism. It is the characteristic diplopia, amaurosis, ptosis or iritis which brings them to Abadie; and the cure of the lightning pains or improvement of an ataxia which may be present is to the patient an incident in the relief of his ocular symptoms.

Milian too reports both complete and symptomatic cures in early cases. He believes, however, that late cases are aggravated by

FIG. 1.

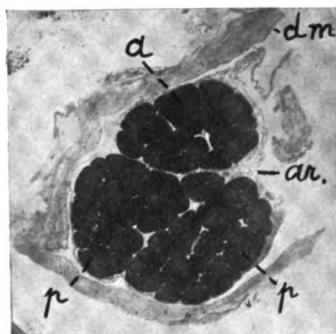


FIG. 2.

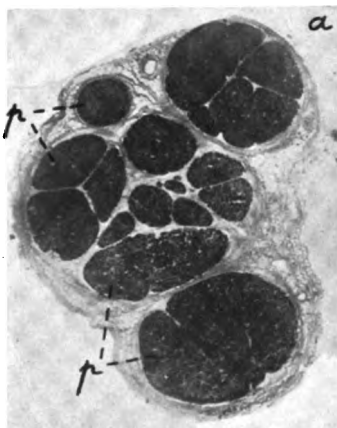
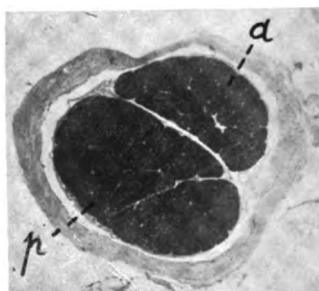


FIG. 3.

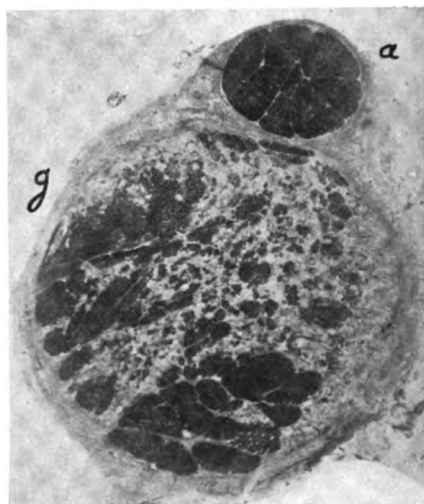


FIG. 4.

FIG. 5.

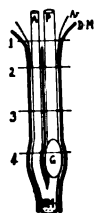
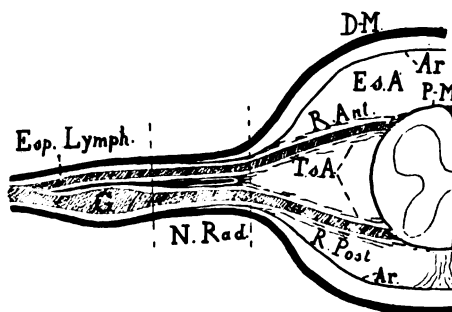


FIG. 6.



For explanation of Figs. 1 to 6, see page 169.

FIG. 7.

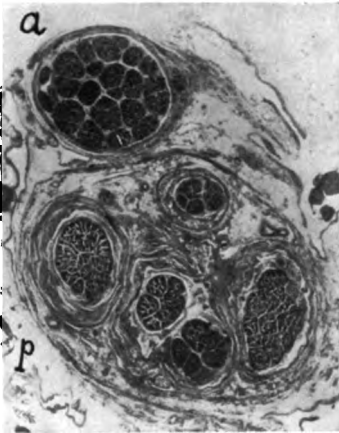


FIG. 8.

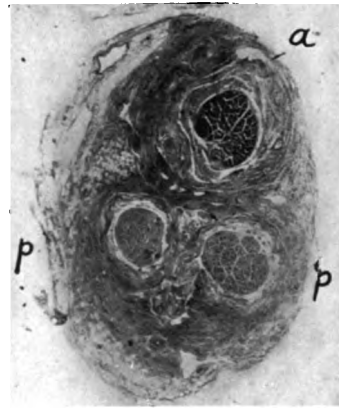


FIG. 9.

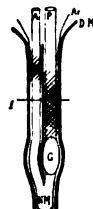


FIG. 10.

FIG. 11.



FIG. 12.



For explanation of Figs. 7 to 12, see page 169.

FIG. 13.

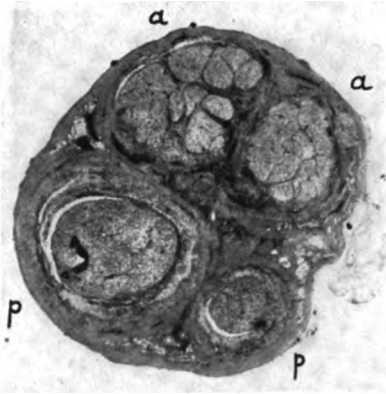


FIG. 14.

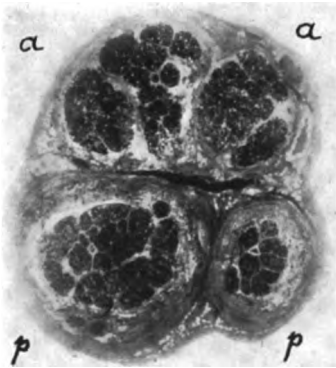
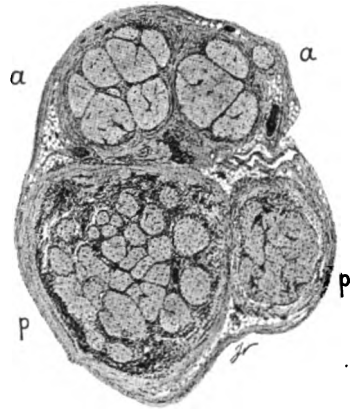
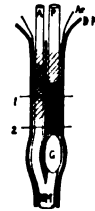


FIG. 15.

FIG. 16.



For explanation of Figs. 13 to 16, see page 169.

FIG. 17.

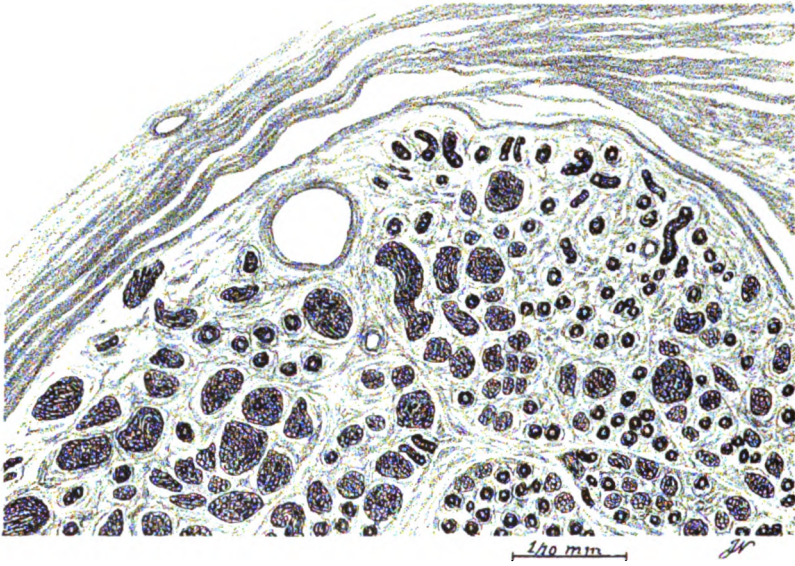
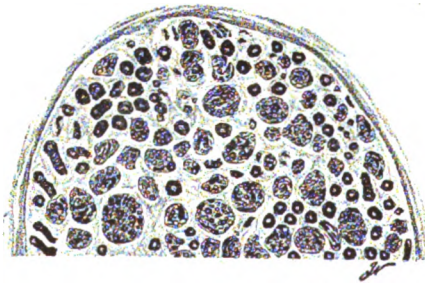


FIG. 18.



For explanation of Figs. 17 and 18, see page 170.

FIG. 19.

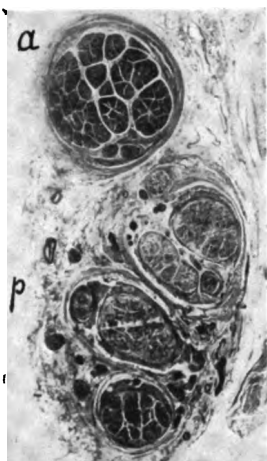


FIG. 19a.

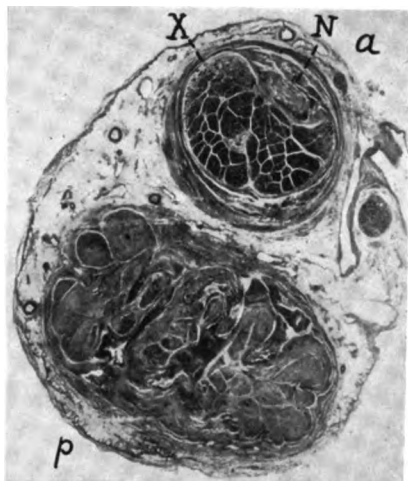
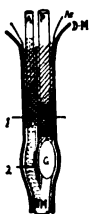


FIG. 20.



FIG. 21.

FIG. 22.



For explanation of Figs. 19 to 22, see page 170.



mercurial treatment. Montagnion and Girond of St. Etienne also report cures; and many other observers in pushing the mercury and introducing it directly into the system are actively testing this method of treatment.

EXPLANATION OF FIGURES

CASE I.—Cross sections of normal second sacral radicular nerve stained by the osmo-tannic method of Azoulay, magnified ten diameters. In Fig. 1 the nerve is not yet surrounded, but in Figs. 2, 3, and 4, the meninges completely surround both anterior and posterior roots, which are separated only by a thin layer of arachnoid. In Fig. 2 the lymph space is clearly manifest, while lower down Figs. 3 and 4 show no space, with this magnification, between the nerve bundles and their enveloping membranes. Fig. 5.—The site of the sections is represented by the lines 1, 2, 3, 4. Note the scantiness of the connective new tissues between the nerve fibres, *D M*, dura mater; *Ar*, arachnoid; *A*, anterior root; *P*, bundles of posterior root; *G*, ganglion. Fig. 6.—Shows the relationship of the meninges to the radicular nerve, *N. Rad.*, radicular nerve; *G*, ganglion; *Esp. Lymph.*, potential lymph space; *R. Post.*, posterior root; *R. Ant.*, anterior root; *P M*, pia mater; *Ar*, arachnoid; *D M*, dura mater; *Es. A.*, arachnoid space; *T. s. A.*, arachnoid trabeculae. The radicular zone of Nageotte is indicated by the two transverse lines. It is here that the meninges form a gutter, and finally a canal in which the nerve runs.

CASE II.—Cross sections of radicular nerves from a case of tabes, same magnification and stain as before. Fig. 7.—First dorsal root at the level indicated in Fig. 11, *P*, posterior root; *A*, anterior root. Note the enormous connective-tissue hypertrophy separating the posterior root into a number of bundles, which are much compressed. The anterior root at this level is relatively healthy, although there is some separation of the nerve fasciculi by the proliferative arachnoiditis so conspicuous in the posterior roots. The lesion of the anterior root occurred, as is the rule, proximally to that of the posterior root. The relative levels are indicated by the cross lines in Fig. 11. The oblique lines indicate the tapering off from inflamed to relatively healthy tissue. Fig. 8.—A similar though more advanced and organized process at level shown in Fig. 12, in the third sacral root. The demyelination of the nerve fibres is more advanced than in Fig. 7, and is most marked on the posterior root, although the perineuritis is quite distinct and extensive on the anterior root, as indicated in Fig. 12. The taking of the stain by these fibres is due to the amount of regeneration which has occurred. Figs. 9 and 10.—Eighth cervical and first sacral segments of the spinal cord of the same case. The lesions of the extrinsic fibres of the posterior columns are clearly shown. Note the healthy fibres in the cornu-commissural zone, and the preponderance of the degeneration, when the cervical region is reached, upon the column of Goll, these being the sacral fibres. Note also in this section (Fig. 9) the unstained zone due to the diseased fibres of the first dorsal root.

CASE III.—Transverse sections of second sacral root from a case of taboparesis stained with hæmatoxylin and eosin to show the round-cell infiltration of the nerve bundles during the endoneuritis which has extended from the perineural arachnoid. It is clearly an inflammation, and not a degenerative process. Fig. 14.—Shows clearly the massive infiltration of the anterior root by the invading lymphocytes (section is through line 1, Fig. 16). Fig. 13.—The organization is proceeding to sclerosis; and much dissociation of the nerve bundles near the ganglion is shown (section through cross-line 2 of Fig. 16). Fig. 15.—The same root near cross-line 1, Fig. 16, stained by Azoulay's method to show how, in spite of the severe perineuritis, many of the fibres, especially of the posterior root, have conserved their myelin.

CASE IV.—Second sacral root from a case of amaurotic tabes, showing the infiltration and organization of the nerve bundles of the anterior root by the endoneuritic process under a magnification of 150 diameters, method of Azoulay. Gradual disappearance of the interstitial neuritis as one descends the nerve. The darker stained fibres are those in course of regeneration. Fig. 18 was made opposite the ganglion through line 2 of Fig. 22, while Fig. 17 was made from the most active zone of the inflammation (line 1). Fig. 19 may be compared with the preceding plates, as it shows the radicular nerve magnified ten diameters. X indicates the region shown in the high-power photograph, Fig. 17. Figs. 20 and 21 show the spinal cord at the fifth cervical and fourth lumbar segments. Note the marked degeneration of the posterior columns, and also the partial demyelination of the right pyramidal tract, as well as the thickened meninges in all the drawings. Fig. 17.—The region marked X in Fig. 19a shows interstitial neuritis with regenerating bundles. Fig. 18.—Section at the level of line 2 in the diagram Fig. 22, showing regenerating bundles. Fig. 19.—Seventh cervical root in the same case, showing the extensiveness of the process.

Anatomy

INVESTIGATION OF THE PORTIO VAGINALIS OF THE UTERUS IN RELATION TO CONCEPTION

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INTRODUCTION

THE cervix uteri plays an important part in impregnation, and slight defects in it may cause sterility. The portio vaginalis is prone to anomalies of several kinds, either congenital or acquired. The most common form of anomaly is hypertrophy of the cervix, which undoubtedly causes the mechanical prevention of entrance of semen. But our present investigation of the portio vaginalis of the uterus is of those cases in which it otherwise appears to be normal and yet there is either some interference with conception or permanent sterility.

Sterility is very annoying to a married woman and often puzzling to the physicians. Sensual gratification is not necessary to conception, neither does its absence preclude conception. The essential condition is that the fertilizing element should have ready entrance to the cervix uteri at the right time. If Velpeau and Rainey are right in their view of the use of the round ligaments in drawing forward the fundus of the uterus, so as to throw back the os uteri into direct relation with the penis during ejaculation, and if this relation is as a rule necessary for impregnation, the reason why women, who are the subject of flexions, displacements and disease of the uterus are so commonly sterile, is partly explained. This relation is absent in many cases where the excessive hypertrophic elongation of the vaginal portion, whether congenital or acquired, offers a decided obstacle to impregnation. Dupuytren, Huguier,

Scanzoni, Lasser, Fritsch, Barnes, and others have reported successful amputation of the cervix for the cure of sterility, and what I have reported here is mainly along the same lines.

ANATOMY OF THE CERVIX UTERI AND ITS RELATION TO THE VAGINA

The uterus is divided into the corpus or body and the cervix or neck, between which is a narrowing or isthmus. This isthmus is very distinct in infants, it diminishes sensibly at puberty, and is still more indistinct after several pregnancies. The vagina being inserted on the neck of the uterus, the latter may be divided into vaginal, middle, and supravaginal portions. The vaginal portion is the symmetrical, unattached part of the cervix, the middle portion is attached to the bladder in front and to the place of the insertion of the vagina behind, and the supravaginal portion is attached to the bladder in front, but is free behind. The word *infravaginal* is sometimes used for the vaginal portion, in contradistinction to the supravaginal. Thus, the latter two portions, middle and supravaginal, of the uterus are in direct relation with the base of the bladder in front, to which they are united by a loose cellular tissue; and are in mediate relation with the anterior surface of the rectum behind, from which they are said to be often separated by folds of small intestine. But Claudius of Marburg states that in the living subject the uterine sound passed into the uterus may always be felt by the finger in the rectum, showing that Douglas's sac is not filled by intestine. In the dead subject, frozen, the uterus with its broad ligaments and ovaries is usually found lying as close to the posterior wall of the pelvis as the lungs are to the ribs. The rectum passes close by the left border of the body of the uterus. Having examined sections of many frozen subjects, he concludes that there is always anteversion, ante flexion, or ante fraction of the uterus when intestinal loops are present in Douglas's sac. My own observations confirm those of Claudius. The anterior and posterior walls of Douglas's sac are always in close apposition in the normal condition.

The vagina is a musculomembranous canal, connecting the uterus with the external genitalia. It runs in an oblique direction forward from its attachment at the cervix to its orifice at the vulva, and is placed between the rectum and bladder. When not artificially dilated, its anterior and posterior walls are in contact with

each other; its transverse section is crescentric at its upper part, H-shaped lower down and vertical at the hymen. It is to be observed that the anterior wall of the vagina is shorter than the posterior wall; the difference being from 1 cm. to 2 cm. This difference in the length of the two walls is produced by the apparent insertion of the cervix into the anterior wall so that the os tincæ faces toward the posterior wall. Between the vaginal portion of the cervix and the reflexions of the vaginal walls lie the fornices of the vagina, which may be distinguished as anterior, lateral, and posterior. The anterior fornix is a guide to the loose tissue between the bladder and the cervix, the lateral fornices lie at the inner aspects of the bases of the broad ligaments and form a guide to the uterine artery and ureter, and the posterior fornix is separated from the peritoneum of the pouch of Douglas by about 0.84 cm. of tissue, the walls of the fornices being everywhere in contact.

The lower extremity of the cervix projects freely into the vagina, and forms the *portio vaginalis*, or vaginal portion of the uterus. It usually projects 0.6 cm. to 1.2 cm., but in certain pathological states it may be lengthened so as to reach the vulva or even to protrude externally. It possesses a transverse aperture, 0.12 cm. to 0.5 cm. in width, termed the os uteri, externum or more frequently the os tincæ from a fancy of the anatomists that it resembled the mouth of a tench. The os tincæ is bounded by two thick lips, of which the anterior is absolutely longer than the posterior. As, however, the distance from the external orifice to the vaginal insertion is only half as great anteriorly as posteriorly, a sensation is communicated to the finger, when an examination is made per vaginam as though the anterior lip were really the shorter of the two. This absolute superior length of the anterior lip, combined with the natural oblique direction of the uterus, causes the external orifice to look nearly directly backward, a fact which is readily recognized when the organs are examined *in situ* by means of a Sims's speculum.

The portio vaginalis of the uterus varies not only in its length, but also in its shape in different women. It also differs in virgins and married women; in multiparæ and nulliparæ. Caseaux says the length of the portio vaginalis diminishes in proportion to the number of pregnancies, and may even disappear altogether in

women who have had many children, but this disappearance is commonly due to senile atrophy. When the portion of the uterus which projects into the vagina disappears, the vagina then terminates in a cul-de-sac, at the bottom of which is felt only a contraction separating the cavity of the vagina from that of the uterus. The vertical diameter of the uterus is divided unequally between the body and the neck. In the virgin, the longest portion belongs to the neck. In multiparous women the two diameters are nearly equal, the difference, if any, being in favor of the body. In multiparæ, the body continues to grow, whilst the neck undergoes an absolute or comparative shortening which reduces its vertical measurement in some cases below that of the body.

The cervical cavity is fusiform in some cases and conical in others, according to the extent of the opening of the os externum. Although the columns of the arbor vitæ are so adapted as to dovetail with each other, there is usually a distinct cervical cavity, the walls not being commonly in close apposition. By making a longitudinal section so as to separate the entire length of the anterior half of the uterus from the posterior, we observe the triangular shape of the cavity of the body with its two superior angles drawn out funnel-wise to be continuous with the Fallopian tubes, and its inferior angle continuous at the isthmus with the canal of the cervix. Below the isthmus is the cervical cavity, fusiform or conical. In multiparæ, in whom the os externum is a wide fissure, the conical form is more manifest in this section than in the antero-posterior section, as it takes in the whole width of the os tincæ; but even in these cases the base of the cone at the os tincæ is commonly more contracted than the middle part of the canal. In nulliparæ the os externum is still more contracted, so that the canal approaches the fusiform character. In many cases of sterility, the os externum is a mere round hole no bigger than the os internum, and the central part of the canal is then generally more dilated than usual, so that it is completely fusiform.

THE STRUCTURE OF THE CERVIX UTERI.—A proper tissue of muscular nature, connective tissue, mucous membrane, glands, vessels, and nerves are the constituent parts of the cervix uteri.

The uterus is composed of muscular fibres of the unstripped variety, arranged in bundles and united by delicate processes of

connective tissue. The arrangement of these muscular fibres has been chiefly studied in advanced pregnancy, when three separate layers, superficial, median, and inner, may be readily distinguished. The superficial layer covers the anterior and posterior surfaces of the uterus like a hood, while the sides are left free. It possesses a membranous thinness, and is intimately adherent to the peritoneum. It consists of fibres which pass transversely across the fundus, and converging at each superior angle of the uterus are continued on the Fallopian tubes, the round ligament, and the ligament of the ovary; some passing at each side into the broad ligament, and others running backward from the cervix into the recto-uterine ligaments. The median layer, which constitutes the great bulk of the uterine walls, presents no regularity in its arrangement, being disposed longitudinally, obliquely, and transversely. The inner layer consists of circular fibres arranged in the form of two hollow cones, the apices of which surround the orifices of the Fallopian tubes, their bases intermingling with each other on the middle of the body of the uterus.

The arrangement of the muscular fibres of the cervix, which is destitute of the inner layer, is somewhat different from that of the corpus. The fibres of the superficial layer in the cervix are generally transverse, but are a little oblique downwards and inwards, and often cross on the median line. They send expansions outward into the broad ligament, backward into the uterosacral ligaments, and sometimes forward into the uterovesical ligaments, while, from the inner layer, in the neck, on the middle of each wall, a branched muscular bundle gives rise to the projections of the arbor vitæ; it rises from the middle of each wall, and forms arches to the right and left. Beneath this bundle, but rather deeply, the fibres are transverse or annular, and are confused with those of the superficial layer.

The connective tissue is abundant around the cervix uteri, forming the parametric tissue proper of Virchow, and also between the posterior bladder wall and cervix uteri, forming an intimate attachment of the two.

The mucous membrane of the cervix is much thicker than that of the body; it is whiter, denser, and less friable. It is 0.1 cm. thick; but this thickness is much increased at the level of the folds

of the anterior and posterior walls. The mucous membrane of the cervix is furnished in its lower third or half with warty or filiform papillæ, 0.2 cm. to 0.6 cm. high which are very numerous on the external surface of the os tincæ. Formed of an amorphous substance containing a multitude of nuclei, they make no projection on the surface of the epithelium. They are, however, well seen when the epithelium is removed by maceration, as suggested by Hassall. Between these folds are seen a multitude of round or oval orifices from 0.3 cm. to 0.4 cm. wide, arranged in linear series and leading to the irregular cavities lined with cylindrical epithelium. The diameter of these cavities, which occupy the whole thickness of the mucous membrane, is scarcely larger than that of their openings. The mucous membrane of the neck is composed of a mucous chorion formed almost exclusively of connective tissue, and of an epithelium formed of cylindrical cells in the upper two-thirds of the cervix, and of pavement cells in the lower third.

According to Sappey the glands of the cervix are branched, not simple tubes or follicles. They are prolonged as far as the muscular tunic, and are far more complicated than is generally supposed. Each is formed of a duct which divides into two or more branches, which again subdivide, and terminate in a cul-de-sac. Their orifices open on the mucous membrane of the cervix at the bottoms of the furrows of the arbor vitæ. They secrete the clear viscid mucus which is usually found filling the os tincæ; and which in the state of catarrh escapes abundantly. Again, we often meet, on the surface of the mucous membrane of the os tincæ, with spherical translucent vesicles called *ovula Nabothi*. These are obstructed muciparous follicles which are found in the cavity of the body as well as in that of the cervix, but which are especially abundant in the neighborhood of the os tincæ. When small they remain buried in the mucous membrane, and only become visible when the mucus accumulates in their cavities through the obliteration of their orifices. When very large they have given rise to the suspicion of serious disease. They are formed of an investing membrane of connective tissue, and of cylindrical epithelium; and contain a transparent, vitreous, or colloid liquid.

The uterine artery, a branch of the anterior division of the internal iliac, passes downward and inward, toward the cervix uteri,

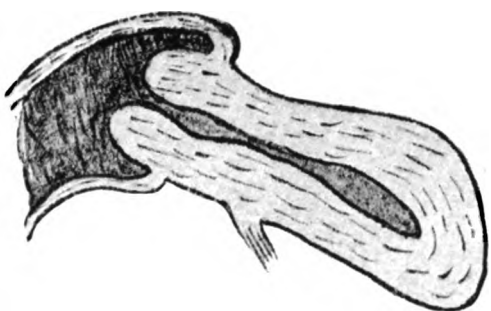


Fig. 1.

Section showing spherical form of the cervix uteri.

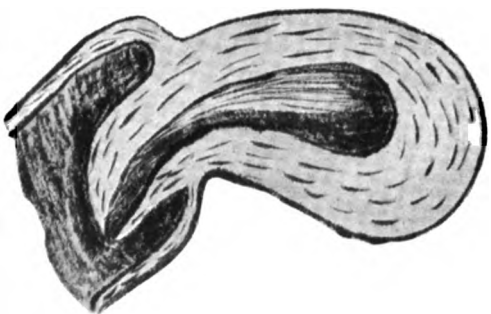


Fig. 2.

Section showing conical form of the cervix uteri.

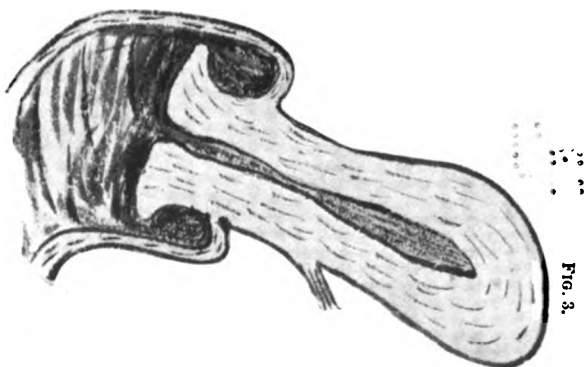


Fig. 3.

Section showing screw-head form of the cervix uteri.

24

giving a well-marked branch to the cervix forming the circular artery, although sometimes several smaller branches take its place. The uterine veins anastomose freely with each other, forming the uterine sinuses or the corpus spongiosum as termed by Rouget, which occupy all the body of the uterus, and cease abruptly at the level of the os uteri internum. Thus, the cervix itself has a much less marked venous development. The lymphatic vessels of the cervix run to the pelvic glands.

In regard to the nerves of the cervix, Boulard does not absolutely decide the question on account of the extreme difficulty of the dissection. He, however, believes that the vaginal portion is not completely lacking in nerves. The supravaginal portion is freely supplied with nerves, but the infravaginal portion very scantily. Hart states that the cervix uteri is supplied with sensory fibres from the third and fourth sacral roots.

INVESTIGATION OF THE PORTIO VAGINALIS IN REGARD TO ITS SHAPE AND LENGTH

In normal construction the cervical canal communicates freely with the vagina by an open transverse fissure; inclining, indeed, to the circular in the virgin. The form of the cervical cavity is thus a flattened cone or funnel, of which the base is open. The vaginal portion projects as a flattened hemisphere scarcely 1 cm. in the vagina, the vagina being reflected off from the cervix a little above the level of the os externum. I have observed three distinct shapes of the cervix in my practice: hemispherical (Fig. 1), conical (Fig. 2), and "screw-head" (Fig. 3) shapes. Gervis says sterility depending upon congenital malformations of the uterus capable of treatment is chiefly associated with those which involve the cervix. One such malformation is undue elongation, which is often of a conical outline, as illustrated in Fig. 2, and projects into the vagina to the extent of 3 cm. or even 5 cm. The os uteri in these cases is generally minute in size, round or "pin-hole" in form, and is often placed, not centrally at the end of the cervix, but rather on one side. In a smaller number of cases, a minute os uteri is found associated with a short and rounded cervix. The third variety, "screw-head" shape, is not congenital, but the result of hypertrophic engorgement of the cervix, and is usually found in nulli-

paræ. There are also marked congenital malformations of the cervix, the stenosis being more frequently at the site of the outer os, less frequently at the inner os; in this latter case it is generally associated with anteflexion of the uterus. Occasionally there is narrowing of both external and internal os, the intermediate canal being of average size; and sometimes, but most rarely of all, there is a distinct constriction in the canal itself. The relation of stenosis of the cervix to the production of dysmenorrhœa is a much debated subject, and need not be entered upon here; but of its influence as a factor in the production of sterility I have no doubt. The accumulated clinical evidence in favor of the view that removal of stenosis facilitates impregnation is, I believe, decisive.

A hypertrophic elongation of the cervix is an occasional congenital defect; and as it simulates prolapsus uteri, it is sometimes called infravaginal prolapse. In these cases the cervix is sometimes so unduly elongated as to reach down to or even to pass beyond the vaginal orifice, and thus to give rise at first sight to the impression that the case is one of ordinary prolapse. The hypertrophic elongation observed in women, married or single, who have never had children, is of a different form, and the cases are not very numerous.

The hypertrophic elongation of the cervix uteri of women who have never borne children may be observed in comparatively young women. In the majority of cases it first comes under observation in married women because before marriage the malformation, for such I believe it to be, lies quiescent. When the enlarged structure comes to be exposed to the contingencies of married life, which include possibly a considerable amount of direct violence, and certainly greater liability to congestion, distress arises. It entails all the inconveniences of a foreign body. It may be compared to a polypus in the vagina. It is usually conical in shape, the base starting from the fundus vaginæ, and tapering somewhat towards its lower end, at the point of which is seen the os uteri. The length of this hypertrophied vaginal portion varies from 2.5 cm. to 5 cm., or even more. The os uteri may come nearly down to the vulva, so that the vaginal canal may be nearly filled with the protuberance. It not uncommonly happens as an aggravation of the trouble that the vagina itself is short.

Other forms of hypertrophy occurring after childbirth may be

said to grow out of the state of congestive hyperæmia and subacute inflammation of the cervix, which takes its departure from labor. The change consists in a slow, localized proliferation of connective tissue. The steps are subinvolution, hyperplasia, exudation of serum into the connective tissue, and proliferation. The cause of this is the laceration of the cervix by parturition, and rarely by surgical procedure—forcible dilatation of the cervical canal. After the receipt of the injury, laceration of the cervix rarely if ever heals spontaneously. Repair occurs by process of cicatrization; the tissue thus formed subsequently contracts; and the underlying cervical structures are distorted. When the laceration is bilateral the resulting contraction of the cicatricial tissue causes a retraction outward of the cervical lips, with consequent eversion of the mucous membrane. The mucous membrane itself, exposed on the everted surfaces of the cervix, presently undergoes glandular hypertrophy, giving to the unpractised eye the appearance of ulceration and abounding granulations. There is no doubt that many of the so-called “ulcerations of the womb,” treated in the years gone by with repeated applications of lunar caustic, were, in reality, but eversions of the endocervix in a state of glandular hypertrophy. The enlarged follicles of the cervical mucosa manifest an augmentation of function corresponding to their abnormal development; and, as a consequence, the cervix is always covered with a clear viscid mucus, sometimes tinged with blood. Changes in the parenchyma of the cervix are equally marked and may present two extremes, atrophy or hyperplasia. When the laceration is comparatively superficial, the resulting inflammation goes through all the consecutive stages from preliminary engorgement to final atrophy; but when the laceration is deep and the consequent cervical eversion is pronounced, there is so much mechanical interference with the circulation, particularly upon the venous side, that passive engorgement ensues, resulting finally in an actual increase of the tissue elements. This state of hypertrophy is sometimes associated with œdematous infiltration; but, as a rule, there occurs an organization of the adventitious tissue elements with consequent enlargement and induration of the cervix. These changes may be more pronounced in some parts of the cervix than in others, the difference being determined by the location, depth, and conse-

quent influence of the laceration. The body and fundus of the uterus, being largely supplied with blood by the ovarian artery, and being drained by the ovarian vein, are not subject to the influences arising in injury of the cervix. It is noticeable, however, notwithstanding the fact that the upper zones of the uterus possess a practically independent circulation, that they undergo the post-partum involutional changes tardily in the presence of deep injuries of the cervix. Glandular hypertrophy is, consequently, not uncommon in these cases in the corporeal endometrium. The inflammations producing this increase in tissue, both glandular and parenchymatous, are manifestly dependent in a large degree upon mechanical disturbances of the pelvic circulation; but, from the fact that lacerations of the cervix never heal without at least superficial bacterial invasion, and that infection once established at the seat of laceration readily extends upward, these inflammations must be recognized as quite as much infectious as traumatic.

INVESTIGATION OF THE PORTIO VAGINALIS IN RELATION TO CONCEPTION

In my clinic, I have been in the habit of measuring the length of the portio vaginalis in all cases coming to the hospital, and have discovered the fact that, other things being equal, the shorter the portio vaginalis is, the more frequently conception takes place. For this cause, I have endeavored to investigate this little point, and thus adopt Gervis's principle for the cure of sterility. Fritsch states that in the healthy subject the portio vaginalis measures from 0.6 cm. to 1.2 cm. in length, and when exceeding this measurement should be considered pathological. Thus I distinguish the cases as three kinds; namely, the first class, those measuring from 0.5 cm. to 1.2 cm.; the second class, those from 1.2 cm. to 2.0 cm.; and the third class, all those above 2.0 cm. in length. With these points in view, I have selected seventeen notable cases each for the first and second classes out of my hospital records. The remarkable results noted in the following tables of these two classes are in favor of my observations. The more remarkable contrast will be observed by comparing the average numbers of each of these two tables. In the table of the first class the average age is 27, the average length of the portio vaginalis is 0.597 cm., the average number of con-

ceptions is 4.53, that is, 26.64 per cent., and the average length of time between marriage and first conception is one year and a little over one month. In the second class, the average age is 29.9, the average length of the portio vaginalis is 1.65 cm., the average number of conceptions is 1.88, that is, 11.04 per cent., and the average length of time between marriage and first conception is

TABLE SHOWING NUMBER OF CONCEPTIONS IN REFERENCE TO LENGTH OF THE PORTIO VAGINALIS.

First Class.

1	2	3	4	5	6	7	8		9	10
Number of patients	Date of examination	Names of patients	Age of patients	Age at first appearance of menses	Age at marriage	Age at first conception	Number of conceptions		Suckling	Length of the portio vaginalis
							Full term	Abortion		
	1899									
1	September ..	H. H.	26	17	18	19	4	..	Yes	0.5 cm.
2	September ..	Y. W.	27	17	20	21	5	1	Yes	0.6 cm.
3	October.....	C. K.	26	14½	19	20	4	..	Yes	0.6 cm.
4	November ..	T. Y.	22	15	21	21	2	..	No	0.55 cm.
5	December...	K. K.	21	15½	18	19	3	..	No	0.7 cm.
	1900									
6	January	N. U.	24	14	18	19	3	..	Yes	0.6 cm.
7	February ...	R. O.	22	15	20	20	2	..	Yes	0.8 cm.
8	March	H. Y.	20	17	17	18	3	..	No	0.5 cm.
9	April	T. I.	33	16	16	20	7	4	Yes	0.5 cm.
10	October.....	T. N.	32	14	20	21	3	2	Yes	0.6 cm.
11	October.....	T. O.	22	16	18	19	2	1	Yes	0.5 cm.
	1901									
12	February ...	T. S.	26	15	18	19	3	1	Yes	0.5 cm.
13	August	T. I.	26	14	18	19	3	2	Yes	0.6 cm.
14	October.....	Y. I.	27	16	21	22	3	1	Yes	0.6 cm.
15	October.....	S. A.	28	15	21	22	5	..	No	0.5 cm.
16	September ..	Y. Y.	41	14	19	20	3	2	No	1.0 cm.
	1902									
17	January	F. N.	35	17	17	19	6	2	Yes	0.5 cm.
	Averages		27	14.94	18.76	19.88	4.53		..	0.597 cm.

three years. Moreover, in those of the third class, the remarkable condition was found that conceptions immediately followed the operation.

TREATMENT

If in women of the child-bearing period the portio vaginalis measures more than 2.0 cm. in length she should be subjected to

operation. If such elongation is due to hypertrophic and hyperplastic conditions resulting from laceration Emmet (*Trans. Am. Gynecol. Soc.*, 1897) believes that these conditions should be subjected to preliminary local treatment, consisting of douches, eliminative tamponade, alterative topical applications, or even local depletion by puncture. Treatment of this kind may so far reduce

TABLE SHOWING NUMBER OF CONCEPTIONS IN REFERENCE TO LENGTH OF THE PORTIO VAGINALIS.

Second Class.

1	2	3	4	5	6	7	8		9	10
Number of patients	Date of examination	Names of patients	Age of patients	Age at first appearance of menses.	Age at marriage	Age at first conception	Number of conceptions		Suckling	Length of the portio vaginalis
							Full term	Abortion		
	1900									
1	March	R. N.	24	16	18	23	1	..	Yes	1.5 cm.
2	May	C. K.	25	16	18	24	1	1	No	1.3 cm.
3	August	H. M.	24	15	16	17	1	..	No	1.5 cm.
4	August	H. Y.	24	16	18	19	2	..	Yes	1.4 cm.
5	August	N. M.	34	17	20	24	1	1	No	1.5 cm.
6	September ..	H. K.	34	16	23	24	1	..	No	1.6 cm.
7	September ..	S. A.	32	18	18	22	1	1	No	1.5 cm.
8	October	N. A.	37	17	20	23	1	..	No	1.7 cm.
	1901									
9	March	T. M.	24	15	19	20	1	..	Yes	1.8 cm.
10	April	K. T.	26	14	19	20	1	3	Yes	1.5 cm.
11	May	M. S.	29	16	20	20	1	..	Yes	1.8 cm.
12	June	M. Y.	27	15	21	23	1	..	Yes	2.0 cm.
13	June	S. B.	31	16	17	30	1	..	Yes	2.0 cm.
14	August	M. O.	43	15	17	18	4	2	Yes	1.5 cm.
15	October	N. S.	40	16	21	25	3	1	No	1.7 cm.
16	November ..	M. S.	27	14	22	26	..	1	No	2.0 cm.
17	November ..	S. A.	28	18	23	24	1	..	No	1.8 cm.
	Averages		29.24	15.88	19.41	22.47	1.88		..	1.65 cm.

hypertrophy that amputation is unnecessary. For amputation, Emmet's operation may be adopted. He first draws the uterus down by gentle and steady traction to the vaginal outlet, always taking care to avoid a jerking movement which would be liable to rupture some blood-vessel, especially if there has been a pre-existing intrapelvic inflammation. The cervix is then steadily held by an assistant just within the vaginal outlet, for at this point the arteries

will be placed sufficiently on the stretch to lessen their calibre, and thus to render the operation to a great extent bloodless. Care is taken to determine accurately the line of vaginal junction, since the bladder will be entered in front and the peritoneal cavity behind, if an attempt is made to remove what seems to be the cervix over which a mass of thickened vaginal tissue has been crowded. In those

TABLE SHOWING NUMBER OF CONCEPTIONS IN REFERENCE TO LENGTH OF THE PORTIO VAGINALIS, AND RESULT OF OPERATION.

Third Class.

1	2	3	4	5	6	7	8		9	10
Number of patients	Date of examination	Names of patients	Age of patients	Age at first appearances of menses	Age at marriage.	Age at first conception	Number of conceptions		Suckling.	Length of the portio vaginalis
							Full term	Abortion		
1	1900 * May	M. M.	28	15	18	19	..	1	..	3.5 cm.
	1904 May	M. M.	32	15	18	29	3	..	No	0.5 cm.
2	1900 * November ..	Y. U.	29	16	16	3.2 cm.
	1094 May	Y. U.	33	16	16	30	1	1	No	0.5 cm.
3	1901 * June	Y. T.	28	15	16	2.7 cm.
	1904 March	Y. T.	31	15	16	29	1	..	Yes	0.5 cm.
4	1901 * November ..	T. Y.	33	16	21	2.8 cm.
	1905 October	T. Y.	35	16	21	35	1	..	No	0.5 cm.

* Date of operation.

cases in which atrophy takes place, as stated before, the field of operation cannot be a large one at the beginning. An incision is now made around the cervix about 0.6 cm. away from the vaginal juncture; the subsequent dissection being made by cutting always toward the centre as a precaution against entering the bladder and the peritoneal cavity, and with the object of removing a cone-shaped piece of tissue. As the operation advances, the denuded area must

continually be drawn up to the vaginal level so that the operator may have the parts under observation and the bleeding under control. As each blood-vessel is divided, the neighboring tissues should immediately be seized by an assistant and held as a fresh point for traction, when the vessels will promptly retract and cease to bleed. The cervix is to be removed segment by segment until underlying healthy tissue is reached. The most efficient instrument for this purpose is the pointed scissors which Emmet devised nearly thirty years ago for clearing out the angles in the operation for laceration of the cervix. After having removed the tissues in the manner just described, non-absorbable sutures are inserted—Emmet employs silver wire. The sutures are inserted antero-posteriorly. Those to either side of the cervical canal are inserted through the posterior lips into the excavation, into the tissues at the fundus of the excavation, out again, and then through the anterior lip of the wound. The other sutures are introduced through the posterior lip of the wound, out again, in again through the posterior lip of the cervical canal, and out through the cervical canal. Another suture is passed similarly to the last, through the lip formed by the anterior wall of the cervical canal, out again, and through the anterior lip of the cervix. As many anteroposterior sutures are passed transversely to the cervical canal as may be required. If we follow the course of either of these sutures it will be apparent that when the front suture, for instance, is twisted, the free vaginal surface must be drawn over the stump, and as the edge of the uterine canal is a fixed point, the former will be secured at that point, and a similar effect will be produced posterior to the cervical canal when the posterior suture has been twisted in the same manner. The result of thus securing these sutures will be that the edge of the divided mucous membrane on the vaginal surface, front and back, will be rolled over in contact with the edges of the uterine canal, and when primary union has taken place the natural calibre of the passage must be preserved. But before securing these, or any of the sutures, as many as may be deemed necessary should be introduced on each side of the cervical canal. Here first the loose vaginal edge is caught up, and then the needle is made to include a sufficient portion of the uterine stump on a line with and lateral to the uterine canal, and in turn it should take up the vaginal tissue behind. The only difficulty is in catching up

enough of the uterine tissue in the centre of the stump to hold it firmly in contact with the flaps after the sutures have been secured. The difficulty can be overcome by using a properly shaped needle with the pointed end slightly bent on itself. The passage of the needle is greatly facilitated by snipping with pointed scissors a sulcus in the tissues at a sufficient depth in front of the advancing needle, and from the bottom of this cut its point should be brought out to pass over to secure the vaginal edge.

After all the silver sutures have been twisted it will be made evident by the introduction of a uterine sound for half an inch that the canal has been left fully open, and it will be seen at the same time that the vaginal tissues have been drawn over the stump and firmly secured to its surface.

At the completion of the operation it is necessary that the uterus should be carefully replaced with the fingers in its natural position, and it must be done without displacing the ends of the sutures, which have been carefully bent down on to the vaginal surface. As soon as the uterus is replaced in its normal position the lateral traction then exerted in the vagina will keep the vaginal covering in close relation with the stump.

No surgical operation with which I am familiar yields a more uniform and satisfactory result than this one, when performed under the following conditions: The proper use of silver sutures, keeping the patient in bed for three weeks after the operation including the menstrual period when possible, and not removing the sutures before the nineteenth or twentieth day, when the parts will have become firmly united and the uterus greatly reduced in size.

REPORT OF CASES

CASE I.—Mrs. M. M., *aet.* 28, menstruation begun at 15, married at 18. Her family history is good. At the age of 19 years, she had an abortion at the sixth month. She has never felt well since, and suffers from leucorrhœa.

May 19, 1900, she came to the hospital. On examination, she is a well-built and fairly nourished woman. The cervix uteri presents a slight erosion and congestion, measuring 3.5 cm. in length.

As usual, I have ordered the preliminary treatment to take away the congestion and engorgement of the part for more than a

month. Although the symptoms subsided remarkably, the length of the cervix uteri was not reduced to any extent. Accordingly the operation for amputation of the cervix uteri was undertaken on July 4, 1900, by Emmet's method as stated before. Chloroform was used for anaesthesia, and the operation was performed with a splendid result, the wire sutures being removed on July 25. She was discharged from the hospital on July 31, 1900.

In June of the following year (1901) she gave birth to a girl. In May, 1904, she came to the hospital to give birth to the third child (boy).

CASE II.—Mrs. Y. N., *aet.* 29, menstruation began in February at 16, and she was married in March of the same year. She has two sisters who have been married for some years, but have no children. On account of sterility she came to the hospital for treatment. On examination, November 5, 1900, no abnormal signs could be observed except the congenital elongation of the cervix uteri, which measures 3.2 cm. As soon as she consented to the surgical procedure we started the operation, following Emmet's method, as no preliminary treatment was required in this case. The operation was successfully performed on November 7, 1900, and she made a rapid recovery. The wire sutures were taken off on the twenty-seventh and she left the hospital on the thirtieth of the same month.

She wrote me a grateful letter when she gave birth to a healthy boy on the twenty-second day of December, 1901.

In April, 1904, she came again to the hospital, as she had had a fall from a stair-way and bloody discharge since. Prior to this accident, her menstruation had stopped for three months. On examination, we found that she was 4 months pregnant. Kept quiet in bed to check the hemorrhage, she nevertheless aborted on the fifth of May and was discharged at the end of the month.

CASE III.—Mrs. Y. T., *aet.* 28, menstruation began at 15, married at 16. She is of a nervous temperament. She became hysterical for fear she might be divorced for not having any children. She came to consult me to determine whether she was unfit to be a wife and mother. On examination, she was a well-built woman, but nervous. She was very attentive to every word I spoke. The cervix manifested congenital elongation of conical shape as shown by Fig. 2, measuring 2.7 cm.

She was delighted to consent to operation when I explained the necessity of the surgical treatment. Without the preliminary treatment, Emmet's operation was performed on June 3, 1901, with satisfactory results. The wire sutures were removed on the twenty-third and on the twenty-seventh she was discharged with cheerful spirits.

In March, 1904, she came back to the hospital again, for treatment of rupture of the perineum when she gave birth to a large, healthy boy on May 20, 1902—just about one year after the operation.

CONCLUSIONS

1. Impregnation is a simple mechanism. Sterility is often the result of some simple disturbance of this mechanism.

2. An elongated cervix measuring more than 2.0 cm., either congenital or acquired, makes the entrance of semen difficult and causes congestion of the part from copulation.

3. Other things being equal, the shorter the cervix is, the more frequently conception takes place. Thus, when the cervix uteri measures more than 2.0 cm. amputation is necessary for cure of sterility.

REFERENCES

- CULLINGSWORTH: *Journal of Anatomy and Physiology*, 1896.
 DEUTSCH: *Centralblatt für Gynäkol.*, 1889.
 EMMET: *Trans. Am. Gynecol. Soc.*, 1897.
 FARRÉ: "Uterus and Its Appendages," *Encyc. of Anatomy and Physiology*, 1896.
 FLOWER: *Nerves of the Human Body*, 1872.
 FRANKENHÄUSER: *Die Nerven der Gebärmutter*, 1867.
 GAWROUSKY, V.: Ueber Verbreitung und Endigung der Nerven in den weiblichen Genitalien, *Arch. für Gynäkol.*, 1896.
 GESSNER: *Zeitschrift für Geburtshilfe u. Gynäkol.*, 1904.
 HART: Contributions to the Sectional Anatomy of the Female Pelvis, 1885.
 HENKE: *Topographische Anatomie des Menschen*, 1879.
 HERMAN: A Contribution to the Anatomy of the Pelvic Floor, *Trans. London Obstet. Soc.*, 1894.
 HERZOG: *Archiv für Anat.*, etc., 1898.
 KLEIN: *Festschrift der Gesellschaft für Gynäkologie und Geburt*, 1894.
 LAASER: *Monatsschrift für Geburtskunde*, 1864.
 MINOT: *Human Embryology*, 1892.
 REED: *Text-book of Gynecology*, 1904.
 WALDEYER: Beiträge zur Kenntniss der Lage der weiblichen Beckenorgane, 1892.

Miscellaneous Topics

THE COURSE OF POSTGRADUATE STUDY OF THE AMERICAN MEDICAL ASSOCIATION

BY JOHN H. BLACKBURN, M.D., DIRECTOR

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SINCE the chief aim of the organized medical profession of the United States, as set forth in the constitution of each County and State society, and that of the American Medical Association is "the extension of medical knowledge and the advancement of medical science," the education of the members of this profession is a subject of vast importance.

The organization of this body of men is an accomplished fact, the work of the Association during the last eight or ten years, with the county society as the unit, showing what may be done by systematic, united effort on the part of the members.

The professional standing of each member depends not only on his training in school but the manner in which he carries on his studies after graduation. It is to be regretted that men are still to-day being graduated from some of the cheap schools who are not qualified to take into their care the lives of human beings, but it is further a matter of congratulation to the profession at large that with the co-operation of the State Medical Examining Boards, the Council on Medical Education of the American Medical Association, and the modern, properly equipped medical university, the average graduate of to-day is much better trained for the practice of medicine. Raising the entrance requirements, a longer course and higher standard for graduation, more extensive laboratory and clinical training, the merging of medical schools in teaching centres, the passing of the privately-owned school, and the effort to have the medical school a part of a fully endowed university, are all hopeful signs of the times, indicating that the

graduate of the future will be more thoroughly equipped for his calling.

But what is to be done with the man who graduated one or many years ago, the "legalized" practitioner who is without adequate training? Is his preparation such that he can practise medicine safely and never do any further study, never attend any society meetings?

Osler says, speaking on the educational value of the Medical Society, "But after all the killing vice of the young doctor is intellectual laziness. He may have worked hard at college, but the years of probation have been his ruin. Without specific subjects upon which to work, he gets the newspaper or novel habit, and fritters his energies upon useless literature. Habits of systematic reading are rare, and are becoming more rare, and five or ten years from his license, as practice begins to grow, may find the young doctor knowing less than he did when he started and without fixed educational purpose in life. The man who knows it all and gets nothing from the Society reminds one of that little dried-up miniature of humanity, the prematurely senile infant, whose tabetic marasmus has added old age to infancy. Why should he go to the society and hear Dr. Jones on the gastric relations of neurasthenia when he can get it all so much better in the works of Einhorn or Ewald? He is weary of seeing appendices, and there are no more pelvic viscera for demonstration. It is a waste of time, he says, and he feels better at home, and perhaps that is the best place for a man who has reached this stage of intellectual stagnation."

In discussing the course of postgraduate study, Dr. J. N. McCormack says (*Kentucky Medical Journal*, December, 1907): "When we took up this work eight years ago we found that there were about 50,000 doctors in the United States, out of 120,000, who had never subscribed for a medical journal and who never received one in their office except the *Brief* or some other free copy advertising sheet of this kind. There were about the same number who had no text-books which did not antedate their graduation. In other words, we found that a large per cent. of them, after their graduation, went out and found their location, laid down their books and ceased to study. We were surprised to find

that the percentage of this submerged element, this dead timber, was larger in New York, Philadelphia, Chicago, Louisville and the great centres of population than in the country districts."

Leading members of the profession in different sections of the country, and county secretaries as a rule, realized how difficult it was under the old order of text-book papers and general discussions to arouse and maintain the interest of the members. In several instances, thoughtful men in different societies, working independently of each other, devised for their respective societies more or less complete schemes of practical postgraduate study. It was the gradual development of this idea that led to the establishment through the Department of Organization of the American Medical Association, of this "Course of Postgraduate Study," providing in this way a systematic course of study for the active county societies and endeavoring to arouse an interest in those who are not at work.

THE PLAN

The effort has been made to cover the field of medicine as it will be met by the general practitioner in country or town. Considerable time has been given to the fundamental branches, anatomy, physiology, chemistry and bacteriology, but particular attention is given the practical clinical phases of each subject. Each of the so-called specialties has been drawn upon, that the practitioner may more readily recognize conditions demanding the services of a specialist and that he may keep pace with the rapid progress being made in every branch of medicine.

The cycle consists of four years, each of which is divided into ten months, allowing a vacation of two months each year. A general subject is provided for each month, which is divided into four parts for the four weekly meetings. There is also provided a programme for a Monthly Meeting, which is intended as a clinical review of the subject for the month.

The subjects for the weekly meetings are further subdivided into topics for two or more teachers or leaders, each topic being elaborated somewhat after the plan of the University Extension Courses of Study.

The weekly meetings are intended for Postgraduate Clubs which may be organized, as a part of a regularly organized county

society, at any point in the county where three or more physicians are willing to meet and devote the necessary time and study to the work. For the monthly meeting the entire county society will meet at the most convenient place and use the Monthly Programme.

To those members who are so situated that they cannot attend the weekly meetings or in societies that hold only monthly meetings, it is suggested that the members use the course as a reading course of home study to prepare themselves for the monthly meetings.

General meetings to educate the public regarding the social evil, tuberculosis, sanitation, etc., should be held at intervals, and joint meetings with the druggists, dentists and lawyers may be made of great good to each profession.

As to the benefits to be derived from following a weekly, systematic course of study may first be mentioned the value of the intimate personal association with one's fellow-practitioner. The close social relations that will inevitably result from coming together each week will tend to remove much of the strife and petty jealousy that are so often found in the profession. The habit of reading and studying each day for some definite purpose will also be found of great value, as well as leading to a more careful study of clinical cases. The more frequent use of the laboratory aids, as the microscopic and chemical examination of the urine, stomach contents, sputa, etc., with the more precise methods of diagnosis, may be mentioned as benefits to the individual. In communities where laboratory facilities are limited or absent, some younger member of each society should be encouraged to take up this work, beginning with a limited equipment of microscopic and chemical apparatus, but adding to it gradually. The cost of this could be met by the county society, allowing the members the use of the laboratory aids free of charge, or the better method of having the patient pay the laboratory fee for any examination,—blood, urine, etc.,—could be followed.

One could not estimate the value to the profession of a medical library in each county society in the United States. A library may be started in any society by each member contributing a few books, and each year adding to this, text-books, high-class medical journals and year-books or reviews. The member who contributes

each year will be most apt to study and thus get the greatest good out of the library.

The highest development of this course of study, when followed in an earnest, systematic way by the entire profession of this country for one or two cycles, will go far toward the solution of the problem of organization and education of the graduate physicians of the United States. At present it is hardly possible to attain to the best in many societies with the members working alone, but much benefit may be derived from the services of teachers or specialists from the outside, who will give a series of lectures and demonstrations on some particular subject after it has been studied by the county society in its regular work. In this way there may be developed in each councillor district, at least, a medical centre to which members from all parts of the district may come at intervals for a series of lectures and demonstrations.

Progress of Medicine

During the Year 1909

TREATMENT

BY A. A. STEVENS, M.D.

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INFECTIOUS DISEASES

TYPHOID FEVER.—W. Coleman (*J. Am. M. Ass.*, Oct. 9, 1909) claims that the loss of nitrogen resulting from the fever and toxæmia in typhoid fever can best be prevented by a *high caloric carbohydrate diet*. He has studied patients on a strict milk-diet—2 quarts a day—and found that they lost from 5 to 12 Gm. (75 to 180 grs.) of nitrogen. This loss, he asserts, is greatly reduced when the energy value of the diet is raised. He has had 46 patients on a diet consisting of milk, cream, milk-sugar, and eggs, with small slices of stale bread or toast and as much butter as the patient wished. The daily quantities of these articles were $1\frac{1}{2}$ quarts of milk, 1 to 2 pints of cream, $\frac{1}{2}$ to $1\frac{2}{3}$ pounds of milk-sugar, and from 3 to 6 eggs. Of the 46 patients only one died, though many were suffering from severe forms of the disease. Moreover, it was not unusual for patients to weigh as much or even more when they were allowed to get up (usually about the fourteenth day of convalescence) as when they were taken ill. Coleman concludes that the diet usually allowed in typhoid fever is detrimental to the patient's welfare, and that the amount of food required to cover his energy expenditures may be estimated approximately on the basis of 40 calories per kilogram of body weight per day. In discussing Coleman's paper, Einhorn, of New York, Claytor, of Washington, Stone, of Boston, and Anders, of Philadelphia, advocated a liberal diet in typhoid fever.

S. Strouse (*Am. J. Med. Sc.*, May 1909) reports two series of cases of typhoid fever, in one of which the diet consisted of eggs, toast, thin gruels, custard, junket, and jelly, and the other of milk and albumin water only. The percentage of deaths in the first series (98 cases) was 6.1 and in the second series (149 cases) 12.7. The percentage of relapses in the first series was 18.3 and in the second series 12.7. It is admitted that the fed cases, on the whole, were slightly milder than those in which the liberal diet was not used, and moreover that some of the deaths in the second series were due to conditions that could not have been influenced in any way by diet.

Watters and Eaton (*Boston M. and S. J.*, April 22, 1909) report a further series of cases of typhoid fever treated by the hypodermic administration of *vaccines* made from dead bacilli. They cite the histories of a family consisting of a mother and three children, all attacked at the same time. Two of the children who received vaccines improved rapidly. A rapid fall of temperature was noted soon after the treatment was begun. The youngest child had been the least sick, and was not inoculated. The child became steadily worse, and on the fourteenth day of the disease the temperature was 104.8°. The vaccine was then administered and the temperature fell immediately. The authors state that of 77 cases treated during 1908, 31 received vaccine treatment. The mortality in the patients receiving vaccines was 3.2 per cent. as compared with a mortality of 11.1 per cent. in those not thus treated. D. Semple (*Lancet*, June 12, 1909) also reports favorably on the use of vaccines in typhoid fever. In 6 of the 9 cases treated, well-marked improvement set in after the vaccinations. This improvement was especially noticeable when autogenous vaccines were injected.

PNEUMONIA.—F. Forchheimer (*J. Am. M. Ass.*, Oct. 30, 1909) holds that dilatation of the right heart is a comparatively rare complication of pneumonia and that vasomotor paralysis is the most common cause of death. The first condition is indicated by marked cyanosis, overfilling of the jugular veins, extreme dyspnoea, increased activity of the accessory respiratory muscles, and an increased area of heart-dulness. The simplest treatment is venesection to the extent of from 250 to 500 Gm. (8 to 16 ozs.) of blood.

Vasomotor paralysis is manifested by increased frequency of pulse, sinking of the blood-pressure, pallor, tympanites, delirium superseded by stupor, irregularity of the heart, and collapse. In the prevention of this last syndrome Forchheimer emphasizes the importance of the fresh-air treatment, of the production of sleep, and of the administration of caffeine, 0.1–0.3 Gm. (1½ to 5 grs.) every four hours. After the development of the vasomotor symptom-complex he recommends caffeine-sodiosalicylate 0.2 Gm. (3 grs.) hypodermically three or four times daily, the application of one or two ice-bags to the abdomen, hypodermoclysis or venous transfusion with large quantities of normal saline solution, and the administration every two to four hours of adrenalin (1 c.c. of a 1000 solution) with the hypodermoclysis. This mode of treatment, applied to all kinds of vasomotor paralysis, he asserts, has given him 50 per cent. of recoveries. In discussing Forchheimer's paper, F. Billing's spoke of the efficacy of intravenous injections of digitalis, not of the active principles of the drug, but of preparations of the leaves. Caffeine and camphor he also recommended, but strychnine he had found useless.

J. Musser stated that in the majority of cases he preferred to rely on fresh air, on judicious local treatment, on hydrotherapy, on the regulation of the proper amount of food taken, and particularly on care that the patient is not overfed. He dwelt especially on the importance of regulating the amount and kind of food taken and of washing out the bowel with normal salt solution in the prevention of tympanites. To combat the renal insufficiency, which is so often a forerunner of cardiac symptoms, he advocated the early use of caffeine, and suggested the use of cocaine when the circulatory conditions became more extreme.

A. B. Harris (*Brit. M. J.*, June 26, 1909) reports 11 cases of various forms of pneumococcic infection treated by *vaccines* (dead pneumococci) obtained from the patients' own sputum or blood. Three patients died early from failure of the heart. One man, aged 36, died on the fifth day after receiving inoculations on the third, fourth, and fifth days. A man, aged 58, received an inoculation at 6 P.M. on the first day of the disease, and the next morning at 10.30 A.M. was convalescent. The other 7 cases were of a chronic character and included delayed resolution, joint infection and

empyema. All were benefited by the treatment. The dose, which was given every third or fourth day, or, when necessary, every day, varied from twenty millions of dead cocci in children to from thirty to eighty millions in adults. Harris believes that estimation of the opsonic index is not necessary, that the temperature and physical signs are a sufficient guide in regulating the number of doses, that delayed resolution and pneumococcic infection of parts other than the lungs ought certainly be treated with vaccines, and that an autovaccine is preferable.

T. Leary (*Boston M. and S. J.*, Nov. 11, 1909) has tested the vaccine treatment in 34 cases of pneumonia of the alcoholic type and in 49 cases of the ordinary type. In the first series mortality was 17.7 per cent. Of the second series 15 per cent. came to crisis in 3 days, and but 2 deaths were reported. The total deaths for the 83 cases were 8, or 9.7 per cent. It was noted that rapid relief of toxæmic conditions followed the use of the vaccines, and in cases of active delirium an abatement of the delirium was prompt. W. Willcox and W. P. Morgan (*Brit. M. J.*, Oct. 9, 1909) also report favorably on the vaccine treatment of pneumonia.

DIPHTHERIA.—P. Schönholzer (*Correspondenz-Blatt f. Schweiz. Aerzte*, 1909, xxxix, Nos. 8, 9) compares the results obtained in diphtheria under *antitoxin treatment* in Kronlein's clinic at Zürich during the last 14 years with those obtained during the 14 years preceding the introduction of serotherapy. The total number of cases was 3322, and the mortality 800. The mortality has dropped from 39.7 per cent. in the first period to 13.39 per cent. of all cases in the antitoxin period, and in the cases with operative treatment from 66.16 per cent. to 32.54 per cent., and in the purely medical cases from 14.24 to 6.82 per cent.

H. Méry (*Arch. de méd. d. enf.*, 1909, xii, No. 9) states that 9 children succumbed to diphtheritic paralysis last year in his 622 cases of diphtheria; and 3 others died of the malignant pharyngitis without paralysis. Since then he has increased the dosage in such cases and the results have been much better. He reports 18 very severe cases in which death was warded off by repeated large doses of antitoxin, with 5 others in which ordinary dosage was used, with fatal outcome. His experience confirms the value of this *intensive antitoxin treatment* in the unusually severe cases, keeping up the

remedy during convalescence. While it did not prevent the paralysis entirely, yet the latter never appeared except in a mild form. Méry affirms that there need be no fear of anaphylaxis on this dosage as that is the result of introduction of a small dose of antigen into an organism saturated with antibodies. When the antigen is supplied in large amounts, anaphylactic accidents do not occur, as clinical experience has abundantly demonstrated.

E. Schreiber (*München. med. Wchnschr.*, 1909, lvi, No. 31) has treated 20 cases of diphtheria by the *injection of antitoxin intravenously* instead of subcutaneously. Nineteen of the 20 patients recovered. He found that 6000 to 10000 units produced no ill effects. Even in children, with these doses the temperature fell more promptly than with the subcutaneous administration, and the general condition seemed to improve more quickly. However, no increase in the effect on the membrane was noted.

ERYSIPELAS.—A. Judd (*Med. Rec.*, Feb. 13, 1909) reports 82 cases of erysipelas treated by means of *carbolic acid and alcohol*. In 67 complete remission of symptoms occurred in from 12 hours to 4 days, in 10 recovery was delayed, and in 5 the treatment failed. The treatment consists in painting with a cotton swab the affected area and about half an inch of the surrounding healthy skin with 95 per cent. solution of carbolic acid. This is left until the purple area becomes whitened, when a thorough application of pure alcohol is made until the whitened area becomes pink. No bad results were noted, even though the hairy scalp, eyelids, mucous membrane of the alæ of the nose, and the nipple of the breast were painted, when necessary. He says that marked improvement in both local and general symptoms rapidly follow and that the treatment has no permanent injurious effect upon delicate skins.

WHOOPING COUGH.—E. F. Cushing (*Cleveland M. J.*, Nov., 1909) advises at the onset of treatment keeping the patient in bed for a week or so, even in the absence of complications. At night every window in the child's room should be kept open. The cold fresh air of a winter night, he claims, is by far the most efficient nocturnal sedative for the cough. During the daytime the patient should be indoors as much as possible. To secure quiet, slowness of eating, and an easy control of quantity, and also, to avoid risk of contagion, he believes that the child's meals should be taken in

the nursery and not at the family table. Of drugs, belladonna and antipyrine, with heroin or opium as a sedative, have served Cushing best. Belladonna is to be given, as advised by Jacobi, in doses increased one drop each day until distinct flushing of the cheeks occurs. In children from 6 to 8 years of age 0.4 to 0.5 c.c. (6 to 8 mins.) of the tincture usually produce the desired effect, and this dose should be continued for a long period. When belladonna fails, he prescribes antipyrine, 0.065 Gm. (1 gr.), for each year of the child's age, in solution three times a day after meals. At bedtime an appropriate dose of heroin, paregoric or Dover's powder ordinarily needs to be given.

E. Weill and G. Mouriquand (*Lyon médical*, 1909, xli, No. 34) have used *oxygen* in the treatment of threatened paroxysms of pertussis in 30 cases, and have found it valuable in warding off bronchopneumonia. The cyanosis is removed and the child is relieved, and keeps in good condition throughout. The oxygen must be inhaled freely.

ACUTE AND SUBACUTE RHEUMATISM.—D. B. Lees (*Brit. M. J.*, Jan. 16, 1909) speaks for the *more energetic use of the salicylates*, especially in children, to ward off cardiac complications. The addition of double the amount of sodium bicarbonate with each dose of the salicylate is recommended as helping to ward off unpleasant symptoms. The initial dose of sodium salicylate for an adult, according to Lees, should be 1.0 Gm. (15 grs.) every 2 hours, or 10.1 Gm. (150 grs.) daily; for a child under 7 years, 0.3 Gm. (5 grs.) at a single dose, or 3.2 Gm. (50 grs.) daily; and for a child from 7 to 12 years of age, 0.6 Gm. (10 grs.) every 2 hours, or 6.5 Gm. (100 grs.) daily. The daily dosage should be increased each day, or every second day, until unpleasant symptoms—deafness, tinnitus, vertigo, or vomiting—are produced. Drowsiness in children, an acetone odor to the breath, or acetonuria, with slowing and deepening of the respirations, are danger symptoms. They may be entirely prevented by the relief of constipation and the use of sufficient sodium bicarbonate. A child may need nearly as much salicylate as an adult, as in a child the infection is more virulent and more often affects the heart, and moreover, in a child the drug is more quickly eliminated in the urine. In many cases it is necessary to increase the daily dose to 13.5 to 16.0 Gm. (200 to 250 grs.)

and in some severe cases to increase it to 23.0 to 26.5 Gm. (350 to 400 grs.).

CEREBROSPINAL MENINGITIS.—Favorable reports on the subdural injection of *Flexner and Jobling's antiserum* (described in *INTERNATIONAL CLINICS*, 1909, ser. 19, vol. iv) in this disease continue to appear. Flexner (*J. Am. M. Ass.*, Oct. 30, 1909) himself has collected from various sources 712 cases in which the serum was used. The mortality in this series was 31.4 per cent. In the first two years of life the mortality was 42.3 per cent., which compares very favorably with that of 90 per cent. obtained under the older forms of treatment. The figures also show that early injections are more effective than later ones; thus the percentage mortality in patients in the first-to-third-day period was 25.3; in the fourth-to-seventh-day period, 27.8, and in the period later than the seventh day, 42.1. A. Netter (*Bull. Acad. de méd.*, 1909, lxxxiii, No. 18) is enthusiastic over the benefits of serotherapy, stating that it not only reduces the severity and shortens the course of the disease, but seems to prevent the development of sequelæ. He has found Flexner's serum superior to other makes and advocates its injection in every case suggesting the possibility of epidemic meningitis, without waiting for the results of bacteriologic examination.

F. S. Churchill (*J. Am. M. Ass.*, Sept. 11, 1909) reports a series of 29 cases in which the serum was injected, the mortality being 44 per cent. Of 16 patients receiving the serum within the first week, 6, or 37 per cent., died. Churchill summarizes the main points of his paper as follows: In all cases clinically suggesting meningitis do a lumbar puncture. If the fluid obtained is turbid, immediately inject at least 30 c.c. (1 oz.) of Flexner's serum directly into the spinal canal without waiting for the bacteriologic report on the fluid. If the *Diplococcus intracellularis* be found, repeat the injections for the three or four following days—in severe cases giving the second dose twelve hours after the first. After the first series of doses, wait two or three days and, if necessary, repeat the series. The serum is a specific, and of value in meningococcic meningitis only. It is useless to give it subcutaneously.

L. Vaillard (*Bull. Acad. de méd.*, 1909, lxxxiii, No. 17) also speaks well of serum therapy.

Lang (*Med. Klin.*, Feb. 21, 1909) has studied the figures in two epidemics of cerebrospinal fever at Cologne. During the first and more severe epidemic, 57 cases were admitted to the Augusta Hospital. Fourteen of these were not treated with serum and 13 patients died (92.8 per cent.), 4 of which were dying on admission. Thirty-seven were treated with serum, but not systematically, and of this number 23 patients (62.1 per cent.) died, of whom 1 was dying when admitted, 1 died from septic infection of a puncture wound, and 2 from hydrocephalus. During the second epidemic 24 patients were treated systematically with large doses of serum and of these 9 (37.5 per cent.) died.

FURUNCULOSIS.—Soper (*Pediatrics*, 1909, No. 3) reports very favorable results from the use of *vaccines* in bacterial infections, chiefly furunculosis of staphylococcic origin, in infancy and childhood. The opsonic index was not followed. Twelve patients received on an average two inoculations each; 6 received three, and 2 received one each. Most of the patients were cured in from 1 to 4 weeks; a few were not improved. Stock vaccines seemed to be as serviceable as autogenous vaccines. Usually a dose of 30,000,000 bacteria was given at first, and later this was increased to one of 100,000,000. In older children the dose was increased to 500,000,000.

J. Sellei (*Wien. klin. Wchnschr.*, 1909, xxii, No. 43) also reports good results with staphylococcus vaccine in furunculosis.

His and Zinsser (*J. Med. Research*, 1909, iii) have treated 11 cases of staphylococcic infection, chiefly chronic furunculosis, by the injection of *leucocyte extracts*. Although the condition had lasted, in spite of ordinary treatment, for periods ranging from several months to five years, complete cure is said to have occurred in all but one of the more chronic cases, and in that one there was marked improvement.

TUBERCULOSIS.—E. L. Trudeau (*J. Am. M. Ass.*, Jan. 23, 1909) discusses the two theories relating to the mode of action of tuberculin in tuberculosis. One of these is the "vaccination" theory, which claims, as a result of tuberculin treatment, a greater or less degree of immunity to the tubercle bacillus itself. The "toxin immunization" theory holds that there results an immunity to the toxin of the bacillus. For a working theory Trudeau prefers

the conception of the production of an immunity that is principally antitoxic. If we accept this view, he concludes, as a guide to treatment, instead of measuring the degree of questionable antibacterial immunity by the opsonic index, or attempting to produce it more or less empirically by a series of moderate reactions, the severity of which we cannot in any way control, the main features in our treatment would be: (1) To raise the degree of tolerance to tuberculin to the highest point attainable in each case by an almost imperceptible and long-continued progression in dosage. (2) To avoid general and focal reactions as much as possible and consider them merely as evidences of intolerance. (3) To follow no arbitrary rule as to rate of increase or the maximum dose to be reached, but to be guided merely by the degree of toxin tolerance of each patient as shown by the symptoms, whether the highest individual maximum dose attainable be only a small fraction of a milligramme or a cubic centimetre or more.

Hamman and Wolman (*Johns Hopkins Hosp. Bull.*, August, 1909) report on the value of *tuberculin treatment* among dispensary patients, 57 in number. Of these, 13 were incipients, 16 moderately advanced, and 28 far advanced. Of the whole number, 10 were apparently cured, in 16 the disease was arrested, 12 were improved, 18 were progressive, and 1 (a far advanced case) died. Of the 13 incipients, only 1 was progressive; of the 16 moderately advanced, 2 were progressive; of the 28 far advanced, 16 were progressive (1 died). The average gain in weight was 6½ pounds; the maximum was 41 pounds. The average maximum dose of tuberculin was 0.005 Gm. ($\frac{1}{12}$ gr.), the largest dose was 1.0 Gm. (15 grs.). The early cases and those patients who did well could take the largest dose. In far advanced and progressive cases tolerance was soon reached.

Wendel (*München med. Wchnschr.*, 1909, lii, 13) has had good results from *intravenous injections of atoxyl and tuberculin*. He advises Koch's old tuberculin in doses of $\frac{1}{100}$ to $\frac{1}{10}$ mgm. ($\frac{1}{6000}$ to $\frac{1}{600}$ gr.) intravenously every eighth day and atoxyl in gradually increasing doses from 0.05 Gm. (1 gr.) to 0.3 Gm. (4 gr.) every second day.

B. L. Wright (*Colorado Med.*, Nov., 1909) makes a further report on the efficacy of deep muscular injections of *mercury suc-*

cinimide in tuberculosis (for method see INTERNATIONAL CLINICS, 1909, ser. 19, vol. I). Of 83 patients treated, 89 per cent. were improved and 7 were cured. Of 24 cases of secondary ulcerative tuberculosis of the larynx, cure occurred in 20. In the intervals between the injections the use of potassium iodide, which Wright formerly advised, is discontinued, arsenic trioxide being employed as a substitute.

G. G. Mosely (*Cal. State J. M.*, Sept., 1909) noted the following results in 33 cases in which mercury was used: marked improvement, 15.15 per cent.; slight improvement, 33.33 per cent.; stationary, 24.4 per cent.; failed, 12.12 per cent.; died, 15.15 per cent.

PLAGUE.—Blue (*Journal of Hygiene*, 1909, ix, 1) sums up the measures that have apparently proved successful in the eradication of the plague at San Francisco as follows: (1) Attack upon the habitation and food supply of the rat; (2) destruction of rat burrows and nests; (3) prevention of access of rats to food by concreting stables, warehouses, markets, etc.; (4) exclusion of rats from houses by the use of concrete or other impervious material; (5) filling of rat burrows with strong solution of chloride of lime; (6) disinfection of all places in which either human or rodent cases of plague have been detected.

METABOLIC DISEASES

DIABETES.—Hall (*Qrt. J. of Med.*, July, 1909) has found the results obtained from the use of *codeine* in doses of 0.016 Gm. ($\frac{1}{4}$ gr.) thrice daily, gradually increased to 0.8 Gm. (12 grs.) daily, on the whole, disappointing, although in a small number of cases the effects of gradually increased doses have been favorable over several weeks. He believes that codeine quickly loses its sedative effect and is, therefore, serviceable only for a short period. *Opium* was given in six cases, in three before any other drug was given and in three after the use of codeine. The initial dose varied from 0.01 to 0.065 Gm. ($\frac{1}{5}$ to 1 gr.), thrice daily, and was usually increased gradually, in one case up to 0.8 Gm. (12 grs.) daily. In spite of the fact that one patient died under treatment, the general results were considered to be better than those obtained with codeine. In the three cases in which the latter had ceased to be effective, opium acted favorably.

J. Rudisch (*J. Am. M. Ass.*, Oct. 23, 1909) has found that *atropine* has a more marked influence on sugar secretion than any of the drugs heretofore tried. With it the glycosuria disappears much more rapidly than with a carbohydrate-free diet alone, and when, with cautious increase in carbohydrates in patients whose urine has become sugar-free, sugar again appears, it is often possible to suppress the sugar excretion solely by atropin without reducing the carbohydrates. With the sulphate the initial dose was 0.00043 Gm. ($\frac{1}{150}$ gr.) thrice daily, and this was increased slowly in some cases up to 0.003 Gm. ($\frac{1}{20}$ gr.) thrice daily. Often a third of the maximum dose accomplished all that could be wished. Rudisch found that methyl bromide of atropine was better tolerated than the sulphate of atropine, and that an initial dose of 0.0085 Gm. ($\frac{2}{15}$ gr.), thrice daily, could be safely increased by 0.0045 Gm. ($\frac{1}{15}$ gr.) at a time until 0.035 Gm. ($\frac{8}{15}$ gr.) was being given three times a day.

A. Magnus-Levy (*Das Koma Diabeticum und Seine Behandlung*, Berlin, 1909) in the treatment of diabetic coma insists on the injection of *sodium bicarbonate* in 3 to 5 per cent. solution into the veins; the quantity should be about a litre (1 qt.) and it should be run in slowly, in from a quarter to half an hour. If the patient shows signs of recovery and can swallow, a teaspoonful of sodium bicarbonate dissolved in water or milk should be given every hour or half hour, and he should be encouraged to drink large quantities of milk or mineral water. The great diuresis thus produced helps to clear out the acid. If the patient recovers, the diet for the first week should contain carbohydrates and the quantity of sugar in the urine should be disregarded, but after this he must return to the diet on which he formerly was, since experience teaches that it does not do to relax the dietetic treatment. Magnus-Levy also emphasizes the need of taking large quantities of fat in severe diabetes, and advocates the use of alcohol, 60 to 90 c.c. (2 to 3 ozs.), of spirits daily. He thinks Von Noorden's oatmeal diet worth a trial, although it is difficult to find an explanation. He also urges that the patient threatened with coma should continue to use sodium bicarbonate regularly.

EXOPHTHALMIC GOITRE.—H. J. Vetlesen (*Norsk Magazin for Lægevidenskaben*, 1909, No. 1) has had excellent results in a

large number of cases of Graves's disease from the use of *thymus extract* and *sodium phosphate*, alternately or combined. He prescribes the latter in the dose of 1.0 Gm. (15 grs.) in solution four times a day and gives from 2 to 4 of the thymus tablets three times a day.

Rogers and Beebe (*Arch. Int. Med.*, Nov., 1908) make a further report on the use of their *cytotoxic serum* in this disease. The serum, which is prepared by the inoculation of animals with pure proteids from human thyroid glands, is designed to neutralize by its antitoxic property the effect of the thyroid proteid in the circulation, and to inhibit by its cytotoxic property the secretory activity of the gland. The injection of the pulp of an organ into an alien species, it is claimed, leads to the formation of antibodies to all the proteids thus introduced. Of 246 cases reported by Rogers and Beebe, 227 were of the class favorable to serum treatment—that is, they were early acute cases of a mild or severe form or were subacute with occasional exacerbations. The report shows that 30 per cent. of the patients were cured of subjective symptoms, with objectively nothing more than a gland discoverable on deep palpation. About 50 per cent. of those treated were much improved, 20 per cent. received no benefit, and about 10 per cent. have died. In cases presenting marked secondary changes and certain indications of hypothyroidism it is advisable to give hypodermically pure proteid of sheep's thyroid in conjunction with the antitoxic serum.

J. P. Dunhill (*Brit. M. J.*, May 22, 1909) concludes that every patient with exophthalmic goitre should be treated medically for three months, and if there is continuous improvement medical treatment should be persevered with, but *operation* should be performed as soon as it is recognized that the patient is not improving. As much gland substance should be removed as is necessary to effect a cure, but not more. Usually one lobe and the isthmus should be removed at the first operation and half of the other lobe at an operation some months after the first. Of 88 patients operated on by Dunhill one died, probably because he crushed a lobe before dividing it. In 15 of 52 typical cases a part of the second lobe was subsequently removed. In every one of these 52 cases, excepting, of course, the fatal one, a cure was effected.

All but one of 8 patients with irregular heart-beats and pronounced œdema were improved. In 5 cases of secondary exophthalmic goitre cure was rapid and complete.

G. W. Crile (*J. Am. M. Ass.*, Nov. 13, 1909) states that though he has performed 72 operations for exophthalmic goitre he is not able to compile any statistical table accurately representing the net clinical results. He has seen no patient with the disease, however, who has not been benefited by operation. The majority regard themselves as cured.

H. Moses (*Berlin. Klinik*, April, 1909) finds that the mortality of unilateral strumectomy for Graves's disease has in the course of the last few years been reduced from about 13 to 11½ per cent. He reports very favorably upon the results of operation, but acknowledges that instances of ideal cure in which all the symptoms of the disease disappear are very rare.

Krecke (*München. med. Wchnschr.*, 1909, lvi, No. 1) reports his experience in 17 operations for exophthalmic goitre. His patients are pleased with the results of the operation, but the exophthalmos has not entirely subsided in any case. Eleven patients operated on more than two years ago have been in excellent health since. He had one fatality in his series.

RICKETS.—Schabad (*Zeitschrift f. klin. Med.*, 1909, lxxvii) has examined the calcium metabolism before, during, and after the administration of *phosphorus*. His results lead to the following conclusions: In therapeutic doses phosphorus produces no change in the calcium metabolism of healthy children, but it leads to a well-marked retention in rhachitis. The retention is to be attributed to the increased absorption and the diminished excretion of calcium in the urine and fæces. The retention of calcium may be noted soon after the exhibition of phosphorus (3 to 5 days); after the withdrawal of the drug this retention persists about two months (following its previous administration for two and one-half months). Phosphorus exerts a specific action on rhachitic bones and raises their calcium content, so that the latter approaches the normal.

CRETINISM.—According to A. von Kutschera (*Wien. klin. Wchnschr.*, 1909, xxii, No. 22) the Austrian government since 1905 has been supplying *thyroid extract* free of charge in seven

endemic foci of cretinism with medical inspection twice a year. In 1908 the number of persons still taking the drug was 608. In 677 cases followed to date, marked improvement was obtained in 48.6 per cent., and only 8.6 per cent. showed no benefit. The most striking proof of the efficacy of the remedy is the fact that in 85.7 per cent. of all cases the former dwarf cretin children grew to be taller than the normal standard for their age. As a rule, treatment was restricted to school children; the oldest cretin was 26 years of age. Even after 20, a number of the cretins grew much taller and the other symptoms of the disease became attenuated. One cretin, aged 20 years, grew 11 cm. (4 in.), but then refused to continue treatment as he outgrew his clothes too fast. He did not lose his milk teeth until after thyroid treatment was commenced, although those of the second dentition were in place.

OBESITY.—Von Noorden (*Med. Klin.*, 1909, i, No. 1) refers to two forms of obesity, one due to overfeeding in proportion to exercise, the other to deficiency of thyroid function. In the first the power of oxidation is normal, in the second it is reduced. The influence of the thyroid may be primary or secondary. In the secondary forms the deficient oxidation may be due to an inhibitory action upon the thyroid secretion by diseases of other organs, as the pancreas, ovaries, hypophysis cerebri, suprarenals, or thymus. Von Noorden treats obesity of the first class by a diet of low caloric value with an abundant supply of albumin. Exercise is a valuable adjunct, and oxidation may be increased by the withdrawal of warmth. If dietetic measures fail after a fair trial, he believes that thyroid insufficiency should be suspected. He holds that a careful and systematic *thyroid treatment* is much less taxing to patients than the ordinary dietetic treatment, especially the "starvation cases." He allows his patients on thyroid treatment a liberal diet, especially of proteins. He concludes that dietetic measures and exercise have no effect upon cases of thyroid origin except that of weakening the patient.

DISEASES OF THE DIGESTIVE TRACT

INDIGESTION.—C. G. Stockton (*J. Am. M. Ass.*, Nov. 20, 1909) discusses the value of *digestive ferments*. He states that the great difficulty in obtaining better digestion through the administration of

pepsin in lowered secretion lies in the fact that we are unable to administer hydrochloric acid with it in sufficient quantity to satisfy the demands of the ferment. Though we occasionally find patients who insist that they feel great improvement from taking pepsin, we may satisfy ourselves that this does not depend on any marked improvement in gastric digestion. As to the effect of pancreatic preparations on intestinal indigestion, he has not been able to satisfy himself that intestinal digestion is improved by the use of any ferments whatever. On the whole, he concludes, it must be admitted that the question of the administration of digestive ferments is complicated and is rendered the more uncertain by lack of precise knowledge as to what becomes of them in the digestive canal. In our present state of knowledge, or lack of knowledge, it behooves us to be modest in claiming either good effects or no effects from the administration of these ferments.

HYPERCHLORHYDRIA.—Enriquez and Ambard (*Rev. de méd. int. et de thérap.*, Oct., 1909) have found that a *salt-free diet* has a prompt and marked influence in lessening secretion and relieving pain in hyperchlorhydria. Once established, the effect is durable, the pain subsiding permanently in two or three weeks or at most in five weeks. The vanishing of the pains after the withdrawal of the salt may turn the scale in favor of a benign gastric affection in certain dubious cases.

E. H. Goodman (*N. York M. J.*, Nov. 6, 1909) has repeated Petri's experiments with *hydrogen dioxide* in 15 patients and has found a striking diminution in the quantity of free hydrochloric acid when a weak solution of the drug is substituted for tea in a test meal. A 0.5 per cent. hydrogen dioxide solution was made up in bulk and under the name of "special water" was given to a number of patients who had the usual symptoms of hyperchlorhydria and the results are said to have been most satisfactory, although one patient complained of the "fishy taste" of the water and another said that it made him sick.

INDICATIONS FOR LAVAGE OF THE STOMACH.—C. G. Stockton (*J. Am. M. Ass.*, Dec. 11, 1909) in a paper dealing with the uses and limitations of examination of the stomach contents, wrote as follows upon the value of lavage: The stomach-tube is of the greatest importance in the matter of diagnosis; in treatment it is

often useless and sometimes pernicious. Nevertheless it is at times a therapeutic agent of the greatest efficiency and cannot be replaced by any other measure in poisoning cases, gastrectasis, before operation in obstruction, in some cases of intractable vomiting, in catarrhal gastritis, and, in general, for the relief of an irritable gastric mucosa.

VOMITING.—G. Baehr and H. Wessler (*Arch. Int. Med.*, Jan., 1909) arrive at the following conclusions from experiments undertaken to determine the action and therapeutic worth of *cerium oxalate*: Commercial cerium oxalate is non-toxic; has no inhibitory effect whatever on vomiting of central origin; may inhibit vomiting due to irritation of the gastric mucosa, but only if given in large doses for some time, so as to coat the stomach wall pretty generally; is not absorbed from the digestive tract. Its action is similar to that of bismuth subnitrate and there is no reason for doubting the value of the drug in such conditions as alcoholic gastritis, gastric ulcer, and the irritability of the stomach arising in the course of infectious diseases, but to be effective it should be given in doses comparable to those in which the bismuth salt is given.

GASTRIC ULCER.—E. I. Spriggs (*Brit. M. J.*, April 3, 1909) discusses the relative advantages of the *Lenhartz treatment* of gastric ulcer with the method more generally employed by temporary fasting and the use of nutrient enemata. The principles of the Lenhartz treatment are briefly as follows: Complete rest in bed for four weeks; feeding the patient from the onset of the attack with small quantities of beaten-up eggs and milk, the quantities being increased daily; the application of an ice-bag to the epigastrium; adding to the dietary boiled rice, minced meat, and other semi-solid food after the first week; and the administration of bismuth and iron in suitable form. Spriggs's paper is based upon 33 cases treated by the Lenhartz method and 34 cases treated by ordinary methods. His conclusions are as follows: The Lenhartz method is not more dangerous than treatment by nutrient and saline enemata followed by the graduated milk diet. In these particular cases the recurrence of hemorrhage was less frequent, and there were no deaths. The pain suffered by the patient in the course of treatment is less on the Lenhartz diet. The diet gives far more nourishment than can be introduced into the body by

nutrient enemata, and is, therefore, more desirable in patients who have frequently been for a long time in a state of semi-starvation, or who have suffered a loss of blood, or both. In addition, the Lenhartz treatment enables the patient to take ordinary diet in a much shorter time than the treatment by nutrient enemata. In patients treated by this method rectal injections may be entirely avoided. Lenhartz himself, at the last German Congress for Internal Medicine, reported his success in 295 cases of gastric ulcer treated according to his principles. In 262 cases there had been hemorrhage just before the treatment was begun, but his total mortality was 2.3 per cent. and only 18 patients had hemorrhage after treatment was commenced.

W. von Leube (*Deutsche med. Wchnschr.*, 1909, xxxv, No. 22) replying to Lenhartz, maintains that his experience in 627 cases in which he has applied his "rest cure" have fully confirmed the advantages of his technic while he sees possibilities of danger in following Lenhartz's directions. Fully 90 per cent. of his patients were cured; 8.5 per cent. improved; and only 1 per cent. failed to benefit, while the mortality from hemorrhage was 0.3 per cent. He is convinced that the only way to check the tendency to bleeding is to keep the stomach absolutely at rest. The patient is kept in bed with a single dose of 2 c.c. (30 mins.) of adrenalin solution (1:1000) supplemented by bismuth, an ice-bag over the stomach, an injection of morphine to keep the stomach quiet (never to relieve pain), and complete abstinence from food by the mouth. Only after the stool has lost its admixture of blood and all evidence of bleeding has disappeared, which is usually the case in two or three days, should the administration of liquid food by the mouth be cautiously commenced. Laxatives must be strictly avoided.

E. Mayerle (*Archiv. f. Verdauungs-Krankheit*, 1909, xv. No. 3) reports his results in 61 cases of gastric ulcer in which he employed the Lenhartz method of treatment. The list includes 29 recent, bleeding gastric ulcers, 17 chronic, and 25 uncomplicated recent cases. His verdict is favorable, on the whole, good recovery being noted in 65 per cent., slow recovery without recurrence in 11 per cent., and with recurrence in 14 per cent. In 10 per cent. no benefit was apparent, or it was transient, while in 7.1 per cent. the diet was not tolerated. In no case was any injury apparent from the

diet commenced immediately after the hemorrhage. Occasionally the tendency to hyperchlorhydria seemed to be increased, and in these cases the proportion of albumin in the diet was reduced, while that of fat was increased. In chronic cases with reduced acidity a diet with less albumin, moderate amounts of fats and carbohydrates predominating, answered the purpose better.

K. Grandauer (*Berl. klin. Wchnschr.*, 1909, xlv, No. 24) from his experience at the clinic of Strauss, who has recently warned that the Lenhartz diet requires a certain amount of caution, states that fat, in the form of butter and cream, is one of the most essential factors in the treatment of peptic ulcer associated with hyperacidity and maintains that a course of treatment as for gastric ulcer is indicated in every case of hypersecretion in which there is the slightest suspicion of a tendency to ulcer.

L. A. Bidwell (*Brit. M. J.*, May 29, 1909) states that in a series of 132 operations which he has performed for ulcer of the stomach and duodenum (excluding cases of perforation) there have been 6 deaths, or a mortality of a little under 5 per cent. Of 101 patients upon whom he performed gastro-enterostomy, 3 had a complete return of symptoms, necessitating a second operation. Of 81 patients he was able to trace, 56 per cent. appear to have been absolutely cured, and another 26 per cent. were in almost perfect health.

P. Clairmont (*Mitt. a. d. Grenzgeb. d. med. u. chir.*, 1909, xx, No. 2) reports from Von Eiselsberg's clinic 259 operations for gastric ulcer. The mortality has been reduced in the 12 years covered from 24.5 per cent. to 6.6 per cent., and with posterior to retrocolic gastro-enterostomy from 16.6 per cent. to 3.5 per cent. The ultimate outcome of a gastro-enterostomy is a complete cure in only 52 per cent. of the cases, with improvement in 15 per cent.

GASTRIC CANCER.—Poncet (*Bull. Acad. de méd.*, 1909, No. 12) in the last six years has operated on 137 patients with gastric cancer. On 40, gastrectomy was performed, and on 97, gastro-enterostomy or gastrostomy. The radical operation (gastrectomy) resulted in an operative mortality of 35 per cent. Of 18 patients who survived the operation and could be traced, 40 per cent. died within the first year, chiefly from recurrence of the tumor. Seven patients who lived over the first year died after an average interval

of 20 months from the time of the gastrectomy. The free interval in one case has been three years and a half, and in another as long as five years and ten months.

DYSENTERY.—S. K. Simon (*J. Am. M. Ass.*, Nov. 6, 1909) claims that *ippecac*, properly used, is almost a specific for amœbic dysentery. Under its influence the stools become diarrhœic, soft and pultaceous, and the amœbæ seem to vanish almost at once. To be effective, however, the drug should be administered in pill form, coated to the thickness of about an eighth of an inch with salol. The patient must be put to bed for the first two weeks and his diet restricted to liquids, or, at most, light solids. Castor-oil may be given as an initial purgative and then each evening, after a three hours' fast, the pills of *ippecac* coated with salol are to be administered. A start may be made with 2.6 to 4.0 Gm. (40 to 60 grs.), depending on the length or severity of the infection, but each subsequent evening the dose is reduced 0.3 Gm. (5 grs.) until the limit of 0.6 Gm. (10 grs.) is reached. Following this, Simon has been in the habit of continuing with 0.6 Gm. (10 grs.) each day for the next two weeks. Bowel-flushes of simple saline solution may or may not be employed in connection with the *ippecac* treatment. In discussing Simon's paper T. B. Fletcher, of Baltimore, and G. Dock, of New Orleans, both attested the great efficacy of *ippecac* administered in the manner suggested.

DIARRHŒA.—C. H. Dunn (*Boston M. and S. J.*, Nov. 18, 1909) points out that the treatment of summer diarrhœal diseases should be based on the known facts as to the etiology of the disease. This may, for the four types, be briefly summarized as follows: (1) Acute nervous diarrhœa: castor oil or calomel, temporary dilution of food, paregoric in persistent cases. (2) Acute intestinal indigestion, type of deficient secretion, irritative diarrhœa: castor-oil or calomel, boiled water for twenty-four hours, barley water for a second twenty-four hours, followed by dilute milk modifications, with low fat and casein and high sugar and whey proteid; irrigation of the colon in long-standing cases. (3) Acute intestinal indigestion, fermentation type: castor-oil or calomel, boiled water for twenty-four hours, barley water for the second twenty-four hours; avoid proteid foods, such as albumin-water or whey. It is safest not to begin milk feeding till the third day, and then very cau-

tiously, with modifications, low in fat, whey, proteid and casein. Living lactic acid bacilli are a specific against this disease and are given in ripened fat-free milk or in buttermilk, which is best begun after forty-eight hours; subsequent feeding according to the type of indigestion also present; irrigation of the colon twice daily; anti-dysenteric serum in resistant cases.

Ramacci (*La Pediatria*, Aug., 1909) speaks very favorably of the administration of *protargol* in infantile diarrhoea, especially in the later stages of acute attacks in the more chronic forms of the disease. The author gives brief accounts of 17 cases so treated. He begins with an initial dose per day of 0.5 to 0.65 Gm. (8 to 10 grs.) reaching to a maximum of 1.3 Gm. (20 grs.), and uses syrup and water as a vehicle. He also emphasises the importance of limiting albuminoid food and continuing an almost exclusively hydrocarbon diet.

INTESTINAL PARESIS.—W. B. Bell (*Brit. M. J.*, Dec. 4, 1909) draws the following conclusions in a paper on the *pituitary body* and the therapeutic value of the *infundibular* extract: In shock the prolonged period during which the blood-pressure was raised made it a most valuable therapeutic agent. In uterine atony powerful and prolonged contractions were induced, so that in such conditions as post-partum hemorrhage it was especially indicated. In intestinal paresis, postoperative or otherwise, immediate effects were always obtained. The injections should be given intramuscularly to avoid superficial sloughing from local vaso-constriction. The dose may be repeated with one hour's interval.

BILIARY COLIC.—H. F. Waterhouse (*Lancet*, May 8, 1909) believes that in the treatment of this condition, besides morphine and hot fomentations, *antipyrine*, 0.65 Gm. (10 grs.) every hour until 2.65 Gm. (40 grs.) have been taken, is a very useful drug.

DISEASES OF THE RESPIRATORY TRACT

ASTHMA.—M. Saenger (*Med. Klin.*, 1909, v, No. 26) states that five years' experience has confirmed the benefits of his method of treating asthma by training the patients to breathe and to endure long pauses between the inspirations. One way is to have the patient count and then to take a short breath, or the patient can blow or whistle or play on a mouth harmonica instead of counting.

The aim is to control the respiration and to free the patient from the dread of suffocation during long pauses between inspiration. He should be trained to use his abdominal muscles more in breathing. Another important point is to teach him to control the tendency to cough, as the cough is liable to start the attack of asthma. The general hygiene must be regulated, and the physician must bear in mind that the patient is liable to have other morbid tendencies, which may require correction. These patients are often lacking in will power and are obstinate and capricious, requiring disciplinary measures.

J. Marcuse (*München. med. Wchnschr.*, 1909, lvi, No. 40) confirms Muck's statement in regard to the efficacy of the sudden application of a *jet of cold water to the back of the neck* as a means of controlling an attack of asthma. His experience has shown him that this is one of the most potent means of acting on the respiration. The patient stoops, and cold tap water is poured on the back of the neck from a pitcher holding over a gallon, held about two feet above; this is kept up for from half a minute to a minute and a half, or a strong jet of water is applied through a tube from a hydrant. Marcuse applies the water thus daily or even two or three times a day, when the patient is being systematically treated for asthma.

C. Wall (*Brit. M. J.*, Mar. 27, 1909) in a discussion on the treatment of asthma at the Royal Society of Medicine said that he notes of 23 cases associated with definite nasal defects. After suitable treatment to the nose, in 14 there was marked improvement. In none was complete cure recorded. Of symptomatic remedies he had found potassium iodide, arsenic and stramonium most useful. The last should be given in doses to cause slight toxic symptoms. Morphine was very valuable, but the fear of narco-mania forbade its frequent use.

Hertz emphasized the importance of urging the patient to combat the tendency by an exercise of will power. In his own case an attack could often be greatly lessened if he resolutely persisted in pursuing some work requiring complete concentration of mind.

Spriggs remarked that it was surprising what benefit followed attention to simple hygienic measures, such as abandoning of an evening meal, regular action of the bowels, and avoidance of

fatigue. For the relief of the more severe attacks he had good results from the injection of atropine, 0.00065 Gm. ($\frac{1}{100}$ gr.), repeated in an hour, if necessary.

Boellke (*Med. Klin.*, 1909, No. 8) has found *pyrenol* of much service in the treatment of asthma and emphysema. He prescribes 3 to 4 Gm. (45 to 60 grs.) a day. Pyrenol is said to be a product of Siam benzoic acid and thymol with synthetic benzoic acid and oxybenzoic acid.

CHRONIC BRONCHITIS.—Schäfer (*Deutsche Archiv. f. klin. Med.*, 1909, iv, 376) speaks of the good results obtained in 29 cases of various forms of bronchial affection, especially in long-protracted cases of bronchitis and in bronchiectasis, from *raising the foot of the bed*, as advocated by Quincke. The patients first lie flat in bed on the back with the head turned to one side. When they have become accustomed to this position, the foot of the bed is raised from 8 to 12 inches for 2 or 3 hours every morning. In some of the cases this procedure was also made use of in the evening. The patients were enabled to raise large amounts of sputum by this method, and during the remainder of the day had little or no cough and no expectoration.

HÆMOPTYSIS.—J. E. Squire (*Clinical Journal*, June 16, 1909) makes the following suggestions as to the treatment of hæmoptysis. If the smallest amount of blood staining is noticed in the sputum it should be regarded as a danger sign, and the patient should at once be put to bed. Calomel, 0.13 to 0.26 Gm. (2 to 4 grs.), should be given, followed in the morning by a dram or more of Epsom salt; if necessary this may be repeated in the day. The patient remains in bed for a couple of days, taking the salt each morning, and if no more staining appears he is allowed to get up, beginning with 2 or 3 hours the first day. If the staining continues the amount of milk may be reduced to 500 c.c. (16 ozs.) daily. Acute hæmoptysis is treated by propping the patient up in bed. Amyl nitrite, 0.6 to 1.0 c.c. (10 to 15 mins.), is inhaled. In large hemorrhages, particularly when the nose gets blocked with blood, it may be necessary to put from 2.0 to 4.0 c.c. (30 to 60 mins.) on a piece of lint and hold it over the patient's mouth. In some cases this has been repeated, and the only complaint made was that it produced a feeling of nausea. When amyl nitrite is not at hand, oil of tur-

pentine may be used as an inhalation or given internally. Morphine has given good results in slight cases. It should be a general rule that when the hemorrhage is large and a cavity is known to be present, the patient should be made to lie on the side on which the cavity is located. Subsequent to acute hemorrhage the patient is kept in bed, propped up a little, purgatives are given, milk, one pint, is given daily, and all other liquid foods are cut off as much as possible, and the patient fed on solids. In some cases calcium lactate, 1.0 Gm. (15 grs.), has been given thrice daily for three days, and then omitted for three days, and so on. It is unwise to examine the chest too fully or too frequently during or immediately after an attack of hæmoptysis.

PLEURISY.—Marcou (*Presse méd.*, 1909, xvii, No. 71) makes an exploratory puncture in every case of pleurisy with effusion and if the fluid is free from pus he reinjects it directly again into the subcutaneous tissue through the same needle, which is not withdrawn, the direction of the point being merely altered to bring it into the subcutaneous tissue. These *auto-serum injections* are repeated at intervals of 2 or 3 days, the amount injected generally being from 1 to 5 c.c. (15 to 60 mins.). He has made over 150 injections in 82 patients, and a number have been cured and under observation for three or four years. The good results, which he ascribes to the formation through the injection of the serum of an antipleuritic substance, confirm those previously reported by Tchigaeff at St. Petersburg, Dehio at Dorpat, and others.

Schnütgen (*Berl. klin. Wchnschr.*, 1908, xlv, No. 51) reports good results from intramuscular injections of *fibrolysin* (thiosinamin and sodium salicylate) in the treatment of pleural adhesions. The injections were repeated once or twice a week. He states that fibrolysin should always be tried after the effusion is completely absorbed and signs of beginning adhesions can be made out.

ŒDEMA OF THE LUNGS.—H. Emerson (*Arch. Int. Med.*, May, 1909) believes *artificial respiration* to be more prompt and effective in relieving pulmonary œdema whenever the œdema and cardiac incompetence are of sudden development and due to causes likely to prove of brief duration or removable by appropriate treatment. It affords relief to the overloaded heart muscle while arterial relaxation and cardiac stimulation are being effected by drugs. In œdema,

the result of cardiac failure in pneumonia, or the inevitable terminal feature in chronic endocarditis, naturally such temporary measures cannot be expected to afford relief.

DISEASES OF THE BLOOD

ANÆMIA IN INFANCY.—J. L. Morse (*J. Am. M. Ass.*, July 10, 1909) is of the opinion that the anæmias of infancy are usually of the chlorotic type, although probably not true chlorosis, and that therefore *iron* is especially indicated. Owing to the difficulty of giving iron by the mouth, and since iron is very prone to disturb digestion, he advocates the *subcutaneous administration* of the drug. For this purpose he has found an aqueous solution of iron citrate very serviceable. This can be put up in perles and sterilized, each perle containing a single dose. Though the injection sometimes causes pain lasting from a few minutes to an hour, Morse has never seen it lead to induration or abscess. The injection is given by means of a glass syringe with asbestos packing, fitted with a platinum needle. The average dose is 0.05 Gm. ($\frac{3}{4}$ gr.) every other day. In most of his cases, some very severe ones, the results have been quite satisfactory.

PERNICIOUS ANÆMIA.—H. J. Vetlesen (*Norsk Magazin for Lægevidenskaben*, 1909, lxxx, No. 11), acting on the suggestion of Tallquist and Faust that *glycerin* might combine with the lipoid substance assumed to be responsible for the disintegration of the red corpuscles, forming a harmless product, has given the drug in 2 cases of pernicious anæmia. The first case was very encouraging and in the second administration of 3 tablespoonfuls of glycerin a day, with lemon juice, was followed in the course of two and a half months by an increase in the red cells from 990,000 to 4,760,000, and of hæmoglobin from 20 per cent. to 90 per cent. A gain of 20 pounds in weight was also noted. Practically no other drugs were given.

G. Klemperer (*Berl. klin. Wchnschr.*, 1908, xlv, No. 52) has treated 8 patients with pernicious anæmia by placing them on a mixed diet with as much milk, cream, and butter as they could take. The object of these additions to the diet was to increase the quantity of *cholesterin* in the blood-serum, cholesterin having been shown to possess the power of preventing the hæmolytic action of

certain poisons, as saponin and cobra venom. Improvement was observed in every case, but as the results were not so brilliant as to be wholly satisfactory, Klemperer sought for a better method of treatment. He therefore tried *arsacetin* (the sodium salt of acetyl-amino-phenyl-arsenic acid or acetylated atoxyl), injecting 0.05 Gm. ($\frac{3}{4}$ gr.) subcutaneously in a 10 per cent. solution, and gradually increasing the dose to 0.6 Gm. (9 grs.). The effect on the blood was very marked. The improvement, however, only continues up to a certain limit, and it is then useless to persist with this treatment. If a recurrence sets in later the injections can again be taken up.

LEUKÆMIA.—J. Elischer and K. Engel (*Zeitschr. f. klin. Med.*, 1909, lxvii, Nos. 1–3) report 44 cases of leukæmia, lymphosarcoma, or mediastinal tumors treated with *Röntgen rays* since 1904. They remark that it is impossible to foretell whether enlarged lymph-glands in the neck will develop into simple lymphoma, pseudo-leukæmia, lymphosarcoma, or a tuberculous process, but as the Röntgen rays have a beneficial action in all these conditions they advise early and vigorous treatment without waiting for differentiation. For 10 or 14 days they advise strong daily exposures for 8 or 10 minutes, then suspension of the exposures while the patient's sensitiveness to the rays is determined and the appearance of by-effects awaited. After this period of observation the treatment is continued until signs of improvement or of the inefficiency of the measure become evident. In leukæmia the early commencement of treatment is highly important as in the later stages exposures must be made with great caution. At first short exposures are made to avoid inducing radiotoxic symptoms. It is particularly important not to begin the treatment too vigorously in leukæmia, and to supplement the radiotherapy with hygienic and dietetic measures. The patient must also be kept under observation later and treatment resumed at the first sign of recurrence, even if only objective. Under favorable conditions radiotherapy seems to postpone death for a long time while relieving the patients of their pain. In many cases, however, notwithstanding great improvement, the danger of acute exacerbation seems to be made more impending by radiotherapy. The tissues in time seem to become immune to the action of the rays, which thus lose their influence. There is no

case on record of actual permanent recovery. Of 19 patients with leukæmia, 10 of the 13 with the myelogenous form and 2 of the 6 with the lymphatic form were very much benefited by the treatment.

HÆMOPHILIA.—K. Wirth (*Zentralbl. f. d. Grenzgeb. d. med. u. chir.*, 1909, xii, No. 7) has treated 23 cases of hemorrhage from various causes by the injection of *horse serum* and is thoroughly convinced of the efficacy of the treatment. As a rule, 20 c.c. (5 drs.) of serum is enough, but 40 c.c. (10 drs.) may be injected without harm. The subcutaneous route is preferable unless the intravenous is urgently required. Horse serum is preferable to other sera, and ordinary diphtheria antitoxin may be used, selecting the vials with the latest date, and applying the serum also locally to the bleeding spot. One of Wirth's patients was a boy of 14, known to be hæmophilic, with persistent bleeding from the nose, throat, and gums, which stopped under applications of diphtheria antitoxin locally and injections of from 15 to 20 c.c. (4 to 5 drs.). According to Wirth 20 cases have been published in which injection of serum arrested hæmophilic bleeding more or less completely, and to date only 2 cases have been reported in which no benefit resulted from the treatment.

L. Gangani (*Gaz. deg. osped, e delle clin.*, 1909, xxx, No. 71) reports a case of hæmophilia in which he was successful in arresting the bleeding only after supplementing diphtheria antitoxin with fresh rabbit serum. He injected 20 c.c. (5 drs.) of antitoxin and 75 c.c. (2 ozs.) of rabbit serum in the course of eighteen days.

DISEASES OF THE CIRCULATORY SYSTEM

CHRONIC HEART DISEASE.—H. C. Bailey (*J. Pharm. and Exp. Therap.*, Oct., 1909) finds that *crystalline strophanthin*, administered intramuscularly or intravenously, is a valuable cardiac stimulant when compensation is broken in chronic interstitial myocarditis or any form of chronic valvular disease, but it should be used in this way only in emergencies. It is not suited for continuous use, and when continued stimulation is desired digitalis should be employed. According to Bailey, the daily dose of crystalline strophanthin should not exceed, as a rule, 0.0005 Gm. ($\frac{1}{120}$ gr.), and under no circumstances should this dose be repeated in twenty-four hours, except after careful study of the effects on the circulation.

D. Danielopolu (*Arch. des mal. du cœur des vaisseaux et du sang.*, Nov., 1908) has treated 23 cases of chronic heart disease by intravenous injections of strophanthin (1 mgm. ($\frac{1}{60}$ gr.) in the twenty-four hours). One of the most marked effects was the extreme rapidity with which the drug acted. In some cases a single injection sufficed to relieve asystole, but usually two or more injections were necessary. The author observed, as did Tust and Hoepffner, that in cases of cardiac lesion and chronic nephritis, although the injection of strophanthin had no immediate effect, yet it prepared the way for the action of theobromine, which, given to the same patients before they had received any strophanthin, caused no diuresis.

J. Grober (*Wien. med. Klin.*, Aug. 1, 1909) states that the effect of the intravenous injection of strophanthin may be marvellous. The drug is indicated in cases of sudden failure of circulation, and may be given in doses of 1 mgm. ($\frac{1}{60}$ gr.) at once. If digitalis has been already given, however, this dose will be too large.

G. Liebermeister (*Med. Klin.*, 1908, No. 8), O. Hornung (*München. med. Wchnschr.*, 1908, No. 39), and Flesch (*Wien. klin. Wchnschr.*, 1908, No. 46) also regard strophanthin as an extraordinarily effective cardiac remedy. The small doses which have usually been given of amorphous strophanthin, and the comparatively large doses in which crystalline strophanthin has been recommended has led to the supposition that the amorphous preparation is more powerful and toxic than is the crystalline glucoside. However, the experiments of R. A. Hatcher and H. C. Bailey (*J. Am. M. Ass.*, Jan 2, 1909) seem to indicate that the amount of the official product to be given by the mouth should be twice that of the crystallized, or from ten to thirty or even fifty times that commonly advised. Nevertheless, these writers are careful to state that they are not prepared to advise that the dose be increased to the extent indicated in the present state of our want of knowledge, but the evidence shows the need of careful clinical investigation of the question.

A. Heffter (*Therap. Monatshefte*, 1909, No. 1) has been led by his investigations to regard crystalline strophanthin as the most reliable preparation. He finds that it is not indetical chemically

with amorphous strophanthin, and the amorphous strophanthins (Boehringer's, Merck's, and Schuchardt's) show differences among themselves. On the other hand, A. Fraenkel (*Therap. Monatshefte*, 1909, No. 2), who has recommended Boehringer's amorphous product for intravenous use, is of the opinion that crystalline strophanthin requires to be further investigated as to its applicability for intravenous injection.

R. G. Curtin (*Therap. Gazette*, Nov., 1908) holds that *fluid-extract of cactus grandiflorus*, 0.3 to 0.6 c.c. (5 to 10 mins.) three or four times a day, is an excellent mild tonic to the heart and that it may be used with special advantage in cardiac weakness during convalescence from infective diseases, in Graves's disease, in and after influenza, in cardiac asthma, and combined with nitro-glycerin in elderly persons suffering from cardiac weakness and dyspnoea. His results have shown to him that failures with the drug are due most commonly to adulterations.

A bath in which nascent oxygen is evolved (*perogen bath*), through the agency of sodium perborate and a catalyzer, has been recommended as a substitute for the carbonic acid bath of the Nauheim treatment by Schnuetgen, Winternitz, Fraenkel, Biedert, and others. Scholz (*Therap. der Gegenwart*, 1909, No. 7) has found it most useful in heart affections accompanied by high blood-pressure. Grosse (*Post-Graduate*, Sept., 1909) summarizes the physiologic effects of the bath as follows: It is a neutral bath which acts oxidizingly upon the skin; it has a powerful suggestive influence; it alters innervation by inhibiting paresthesias, by its sleep-promoting properties, and by its general sedative, and indirectly stimulating, action; it is a circulatory revulsive, turning the blood to the inner body, particularly into the muscular area; and it reduces abnormal blood-pressure, probably rendering the blood less viscous.

ACUTE SEPTIC ENDOCARDITIS.—W. G. Thompson (*Am. J. M. Sc.*, Aug., 1909) has treated seven cases of septic (streptococcal) endocarditis by the injection of *homologous* or *autochthonous vaccines* with results that have demonstrated the effectiveness of this method and afford strong hope of even greater success when the technic shall have become better understood. The injections were given at intervals of from one to four or five days, from 50,000,000

to 300,000,000 dead streptococci being injected at a time. Of the cases, three were cured; in two fatal cases the effect upon the septic phenomena was striking and temporarily beneficial, and in two fatal cases it was slight but clearly demonstrable. In several of the cases polyvalent vaccines had been employed, but without success, before homologous vaccines could be obtained. In addition to the seven cases of septic endocarditis, one of advanced pyæmia was cured.

F. Billings (*Arch. Int. Med.*, Nov., 1909) reports a series of 14 cases of chronic infectious endocarditis, 11 of which were of pneumococcic origin, and suggests the following principles of treatment: The treatment should be absolute rest, with good air, sunshine, as much simple liquid and soft solid nourishment as may be given, and the use of those remedies which will conserve the patient's strength and the functions of the organs without too much mischievous interference. Inoculation of patients with their own dead pneumococci was always harmful. Observations of patients injected with even small doses (2,500,000) leads Billings to believe that this form of treatment for infectious endocarditis due to the pneumococcus is not only devoid of benefit, but probably is harmful.

CHRONIC MYOCARDITIS.—S. B. Ward (*Albany Med. Annals*, Nov., 1909) states that in his experience one-drop doses of 1 per cent. solution of *nitro-glycerin*, given with digitalis, every two or three hours, are practically inert; but if from 0.3 to 0.6 c.c. (5 to 10 mins.) be given every minute, for 20 or 30 doses, brilliant results will be obtained days before the effect of digitalis can possibly be expected. In œdema of the lungs the toleration for this drug is most extraordinary, and relief from dyspnoea is uniformly obtained before the physiologic effects, such as flushing and headache, are produced. Ward reports two cases of myocarditis in which nitro-glycerin was of the greatest service.

DILATATION OF THE RIGHT VENTRICLE.—W. H. White (*Clinical Jour.*, Mar. 31, 1909), in a paper on venesection, writes that the great majority of patients for whom *bleeding* is desirable are those in whom the right ventricle is overgorged with blood, most frequently as a result of mitral disease, bronchitis or pneumonia. The common idea that a small pulse is a contraindication he negatives by pointing out that such small pulse is to be interpreted as

signifying that so much blood is dammed back in the venous system that not much gets into the arteries. A cardiac patient who does not respond to digitalis when in a livid condition will respond to it after bleeding.

ANGINA PECTORIS.—T. C. Allbutt (*Brit. M. J.*, Oct. 16, 1909) in discussing the treatment of this disease states that his orders are: Never bring on the pain; every renewal of it keeps up the sum of stimuli. If for this end, absolute rest in bed be required, then bed it must be; with the corresponding reduction of food. The subsequent imprisonment must be determined by the sagacity of the physician guided by the sensations of the patient. At the same time all those measures, medicinal, dietetic, and other, which are known or supposed to reduce arterial pressure must be enforced. Nitrites are indispensable. To guard against vagus inhibition atropine should be administered regularly. In very painful cases morphine may be needed also. An ice-bag applied cautiously and intermittently to the upper thoracic spine may prove helpful. The possibility of syphilis must be considered, and if discovered or even suspected, resolute treatment must be prescribed. Empirical experience suggests that iodides in some doses should be administered in all kinds of the disease. Specific remedies for any general morbid condition as rheumatism, gout, etc., must not be forgotten. Of new remedies two have seemed to be efficacious, more especially in angina minor, namely the high frequency current, and the administration of the lactic acid bacillus by the method of Metchnikoff. Baths and massage cannot be prescribed in any urgent stage of the disease. Causes of eccentric irritation must be discovered and neutralized. Chloroform is very dangerous in angina. In syncopic failure of the heart, artificial respiration should be tried.

DISEASES OF THE KIDNEYS

CHRONIC NEPHRITIS AND URÆMIA.—E. F. Wells (*J. Am. M. Ass.*, Nov. 27, 1909) states that the oncoming of uræmia is manifested clearly by shadows cast before. One of the most significant of these foreshadowings is an occult œdema, in which the intracellular spaces are distended with serum, and to a high tension. The soft parts are resistant to pressure, but without pitting. Such patients may be deprived of the excess of extravascular liquid with the loss of

from 5 to 20, or more, pounds in weight in a few days, and with the loss of weight (due wholly to the loss of liquid) there comes a marked improvement in both objective and subjective symptoms. The following plan of treatment, modified to meet varying and individual conditions, is suggested: During the first day the diet should consist of thin gruels, cream and water, vegetable soups, tea, coffee, cocoa, water and carbonated waters. From these there should be omitted the gruels on the second, and soups on the third day; during the fourth and fifth days very little should be taken; on the sixth day the soups should be replaced, and the seventh the gruels; later the ordinary careful dietary of the nephritic should be gradually resumed. Every night of the first three days give the patient 0.65 Gm. (10 grs.) of blue mass, in two recently made pills of 0.3 Gm. (5 grs.) each, followed by an efficient sodium or magnesium saline in the morning. Beginning on the fourth morning, after free action of the saline, there is given 0.002 Gm. ($\frac{1}{30}$ gr.) pure elaterin hourly for three doses; 0.0027 Gm. ($\frac{1}{24}$ gr.) every two hours for three doses; finally, 0.0036 Gm. ($\frac{1}{18}$ gr.) every three hours (or *p. r. n.*) until ten or twelve watery bowel movements have been induced. During the administration of the elaterin the patient should remain in bed, using the pan. He should also be informed of the abdominal distress likely to follow the use of the drug. During the period of alvine drain, renal activity is reduced; subsequently the flow of urine becomes very free, often continuing so for many days, even until the cardiovascular-sanguinous and lymphatic-tissue lymph-balance of the circulation has been restored. In discussing Wells's paper, D. L. Edsall called attention to the fact that a reduction in the amount of sodium chloride, aside from any influence on oedema, helps largely to lessen the work of the kidneys. He also pointed out that very satisfactory results are sometimes to be obtained in chronic nephritis by placing patients on actual starvation for a brief period, sometimes a day and sometimes several days, using nothing but water, or a pint of dilute skim-milk in the day. J. Tyson confirmed Edsall's statements.

J. H. Musser referred to the use of two drugs. First, iron, which is administered not only for the hypertension but for the degenerative lesions that accompany it. When given for a long period it not only lowers the blood-pressure, but also exerts some

nutritional effect on the cell structures; secondly, opium in small doses gives satisfactory results in securing that equanimity of mind which is so necessary and aids in keeping down the stress incident to increased blood-pressure.

In regard to *restriction of salt*, R. H. Babcock (*J. Am. M. Ass.*, June 5, 1909) states that in his experience if the œdema is soft, restriction or total abolition of salt from the diet will usually prove most effective in reducing the œdema, but in the hard œdemas dechloridization is of small value. In paroxysmal dyspnœa, not the result of any cardiac affection, but probably of toxic origin, restriction of the intake of salt often gives very happy results.

On the other hand, J. W. Blocker (*Deutsch. Archiv. für klin. Med.*, 1909, No. 1) believes that the value of dechloridization in the treatment of nephritic œdema is still an open question. Personally, he has found a salt-free diet rarely of value.

DISEASES OF THE NERVOUS SYSTEM

EPILEPSY.—E. Long (*Rev. de méd.*, 1909, xxix, No. 10), who has had seven years' experience in the treatment of epilepsy by giving bromides in combination with a *salt-free diet*, reports 4 very severe cases in which the treatment was kept up for years with great benefit. He concludes that reduction of the intake of salt materially enhances the action of bromides and believes that some of the accidents ascribed in the past to bromide intoxication have been really caused by casual and unintentional ingestion of less salt than usual.

Cicarelli (*Il Policlinico*, 1909, xvi, No. 6) states that he has had excellent results from the use of *calcium hypophosphite* in the treatment of 25 cases of epilepsy, and so confirms the favorable reports made by other Italian clinicians upon the use of lime salts in this disease. He gives 0.6 to 1.0 Gm. (10 to 15 grs.) of the salt three times a day alone or in combination with bromides.

A. R. Littlejohn (*Lancet*, May 15, 1909) reports marked improvement in a number of patients with epilepsy from the administration of *calcium lactate* in doses of 1.0 Gm. (15 grs.) thrice daily.

A. P. Ohlmacher (*J. Am. M. Ass.*, Aug. 14, 1909) also speaks well of the action of calcium lactate in epilepsy, and states that a hemorrhagic tendency in one of his patients in the Ohio Hospital for Epileptics first prompted the use of the drug.

Bratz and Schlockow (*Deutsche med. Wchnschr.*, 1909, xxxv, No. 27) have employed *sabromin* in 50 cases of epilepsy and find that while the drug does not act better than the old fashioned bromides, it has an advantage over the latter in not readily producing symptoms of bromism. *Sabromin*, which is the dibrom-behenate of calcium, is a white tasteless powder containing about 30 per cent. of bromine. It is not irritant to the stomach and is not absorbed until it reaches the intestine. Its action is less rapid but of longer duration than that of the alkaline bromides.

J. von Mering (*Med. Klin.*, 1908, No. 38), S. Kalischer (*Deutsche med. Wchnschr.*, 1908, No. 40), and A. Eulenberg (*Med. Klin.*, 1908, No. 45) also have had good results with *sabromin* in epilepsy. The usual dose is 1 Gm. (15 grs.) three or four times a day.

NEURASTHENIA.—Boas (*Zeitschr. f. Balneolog.*, 1909, ii, No. 1) emphasizes the value of periods of relaxation (*Ausspannungen*) in the treatment of neurasthenia. He sends patients away from home for five or ten days at intervals of six or eight weeks, and has been astonished at the benefit obtained in many instances. The neurasthenic conditions resulting from excessive mental work or emotional strain are the ones most likely to be improved by these brief relaxation trips. Boas points out that it is not necessary for the patient to go to a health resort, as a trip to another city, where there is opportunity for attending theatres, concerts, museums, etc., answers the purpose. The main thing is to have the *ausspannungen* repeated systematically every six or eight weeks.

CHOREA.—At the last meeting of the British Medical Association, E. Wynter (*Brit. M. J.*, Sept. 18, 1909), in the discussion on the neuroses of children, called attention to the great value of *chloretone* (chloroform-acetone) as a cerebral sedative in the neuroses, especially in acute chorea, and stated that the routine use of the drug had reduced the time necessary for the suppression of the movements to an average period of nine days. He had observed slight erythema and desquamation of the skin to follow the use of the remedy in several cases. In chronic cases the results were not nearly so good. Coutts and Leslie also spoke favorably of the action of *chloretone* in acute chorea.

TRIFACIAL NEURALGIA.—Testimony to the value of deep injec-

tions of alcohol in the treatment of trifacial neuralgia continues to appear.

Purves Stewart (*Brit. M. J.*, Sept. 25, 1909) states that out of 15 cases of the most severe type, some of them in patients of advanced age, 12 (80 per cent.) have been entirely relieved for periods varying from twelve months downward. He concludes that while the method does not effect a permanent cure in every case, it affords relief for prolonged periods, and is, moreover, free from the pain, risks, and serious deformities of the major operation on the Gasserian ganglion.

W. Harris (*Brit. M. J.*, Dec. 4, 1909) reports 24 cases of true trigeminal neuralgia treated by injection of 80 per cent. alcohol. Of this number, 20 appeared to have been completely successful, and 2 of the remaining four partial failures.

Victor Horsley in discussing the subject advocated the alcohol treatment with the view to avoiding the Gasserian operation. He had found the best results in the cases in which the pain was strictly localized to one division of the nerve. His general procedure was to recommend the injection of alcohol first, and afterwards, if necessary, resort to the removal of the ganglion. In 149 cases in which he had removed the ganglion the death-rate was 7 per cent., and of patients under the age of 50 he had not lost one.

Hugh T. Patrick (*J. Am. M. Ass.*, Dec. 11, 1909) reports 75 cases of trifacial neuralgia treated by deep injections of alcohol and of this number the results were negative or doubtful in but 8. Patrick makes the injections with a straight needle about 10 cm. long, 1.5 mm. thick and fitted with a stylet or obturator, the blunt end of which is flush with the needle point. The needle is introduced at the lower border of the zygoma, the object being to reach the inferior maxillary division of the nerve at its emergence from the foramen ovale (about 4 cm. (1 in.) deep) and the superior maxillary as it leaves the foramen rotundum (about 5 cm. (1½ in.) deep). Deep injections for the supra-orbital branch he has abandoned as being too hazardous, and when an injection of this branch is needed he uses a "peripheral" injection at the supra-orbital notch. The solution recommended is 85 per cent. alcohol with 4 grains of cocaine to the ounce (1 to 120). An anæsthetic is very rarely necessary. The only complications were a small hæmatoma

and transient paresis of the sixth nerve in a few instances. A good injection, as shown by marked analgesia, may be expected to relieve for from 1 to 3 years.

J. Flesch (*Centralbl. f. Grenzgeb. d. med. u. chirurg.*, 1909, xii, No. 16) also adds his commendation to that of other writers.

SCIATICA.—A. Bum (*Wien. med. Klin.*, July 25, 1909) has obtained good results from the infiltration treatment of idiopathic cases of subacute and chronic (not acute) sciatica. He considers the action to be purely mechanical, and recommends sterile isotonic salt solution, introducing 100 to 120 c.c. (4 oz.) under stronger pressure into the sheath of the nerve. The needle is entered at the point at which the long head of the biceps emerges from the lower border of the gluteus maximus, the patient's bent knee being meanwhile supported. The cannula, 10 cm. (4 in.) in length, is pushed at right angles for about half its length, the proximal end is then lowered, while the needle is pushed in from 3 to $3\frac{1}{2}$ cm. ($1\frac{1}{2}$ in.) further, the object of the change of direction being to insure that the needle travels along the sheath in the direction of its length rather than simply piercing the sheath. In 274 cases treated by Bum, 169 were permanently cured, 54 were improved, 13 relapsed, and 38 were not benefited.

TETANY.—T. P. Kinnicutt (*Am. J. M. Sc.*, July, 1909) reports a case of tetany, the consequence of gastrectasis, in which the spasmodic symptoms were completely controlled by the continuous use of *calcium lactate* (4 grammes in 1000 c.c. of normal salt solution) administered intravenously. Parathyroid preparations were without effect. Death ultimately resulted from the inanition caused by the pyloric stenosis.

DISSEMINATED SCLEROSIS.—G. Marinesco (*Arch. d'élec. med.*, June 10, 1909) records two cases of disseminated sclerosis in which considerable benefit ensued from the application of X-rays. In a third case of very advanced disease no good effects were observed. Marinesco states, that he was led to employ this method of treatment because favorable results had been obtained by Raymond and others with X-rays in cases of syringomyelia.

MEDICINE

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INFECTIOUS DISEASES

TUBERCULOSIS.—Smithies and Walker (*J. Am. M. Ass.*, Jan. 2, 1909) report 450 cases of the conjunctival test for tuberculosis, and give an extensive bibliography. They emphasize the harmlessness of the test when the eye is normal and the reagent has been prepared according to Calmette's method; it is also rapid, convenient, and inexpensive. A positive reaction occurring promptly usually denotes an active tuberculous focus together with a good systemic resistance. If the reaction is delayed or there is little change in the conjunctiva the prognosis is unfavorable.

Lawrason Brown (*J. Am. M. Ass.*, Jan. 30, 1909) discusses the classification of tuberculous patients and statistical reports of sanitariums. He advises as the most satisfactory for chronic cases the following:

ON ADMISSION

Incipient.—Constitutional symptoms and sputum, slight or absent; infiltration limited to a small area; no complications; bacilli (sputum) either present or absent.

Moderately Advanced.—No marked local or general impairment of function; moderate consolidation; no serious complications.

Far Advanced.—Marked impairment of function, local and general; either consolidation of an entire lobe, beginning scattered cavity formation, or serious complications.

ON DISCHARGE

Apparently Cured.—Constitutional symptoms and expectoration with bacilli absent for 3 months; the physical signs those of a healed lesion.

Arrested.—No constitutional symptoms for 2 months; physical signs stationary or retrogressive for 2 months.

Improved.—Slight or no constitutional symptoms; physical signs stationary or improved; cough and sputum with bacilli usually present.

Unimproved or Progressive.—Signs and symptoms unabated or increased.

Died.—

ULTIMATE RESULTS

Cured.—No constitutional symptoms nor sputum with bacilli after 2 years of ordinary life.

Well.—Patients who would be classed *cured* except that no information as to sputum is available.

Arrested.—(As on discharge).

Improved.—(As on discharge).

Progressive.—(As on discharge).

Died.—

Marmorek (*Presse méd.*, Jan. 2, 1909) advises fixation of complement as a much more satisfactory test for active tuberculosis than the tuberculin reactions, as there is not the danger of error in case of latent foci. The toxin generated by the active tubercle bacilli, he states, is not the same as tuberculin, and may be found in the serum and urine. By adding either of these to the serum of a horse immunized against tuberculosis the complement is fixed and hemolysis occurs, while the serum or urine from a normal individual does not have this effect. As a result of examining 600 cases it is stated that the test is very reliable, a positive reaction being obtained only very rarely where the clinical findings do not indicate tuberculosis.

E. R. Baldwin (*J. Am. M. Ass.*, Feb. 20, 1909) concludes, from the results of 1000 conjunctival tuberculin tests made with 0.3 per cent. and 0.5 per cent. solutions of old tuberculin precipitated by alcohol and instilled with carefully calibrated droppers, that the Calmette reaction is of value in confirming a diagnosis of early tuberculosis, but is not of much value when the symptoms are only suspicious, and is of no use in prognosis. The danger of injury to the eye is slight under proper precautions, but the advantage of repeating the test in the other eye is so slight that it is not to be recommended.

Martin (*München. med. Wchnschr.*, Jan. 19, 1909) finds that a negative Calmette reaction in tuberculosis during pregnancy is an important sign of weak systemic defence, and an indication

for terminating the pregnancy in order to give the patient a better chance to combat the disease.

W. L. Moss (*Johns Hopkins Hosp. Bull.*, Feb., 1909) discusses the relationship of bovine to human tuberculosis. In 300 cases of tuberculosis in which the type of bacillus has been determined the bovine form has been found in 20 per cent., but in many of these the infection may not have been directly from a case of tuberculosis in cattle, as the bovine bacillus may retain its type in spite of a sojourn through several human beings. Autopsy evidence is very conflicting, but clinical evidence, although not absolute, points strongly to the assumption that tuberculous cattle are a very real menace to human beings.

A. Wolff-Eisner (*J. Am. M. Ass.*, Feb. 20, 1909) emphasizes the advantage of the conjunctival reaction in differentiating active from latent cases of tuberculosis, whereas the cutaneous and subcutaneous reactions are often positive in the case of quiescent foci as well as in that of active lesions.

H. S. Patterson (*Arch. Int. Med.*, May, 1909) concludes that the Moro reaction is to be preferred to the Pirquet reaction as it is more suitable for adults and is entirely free from danger.

Hamman and Wolman (*Arch. Int. Med.*, 1909) find as the result of a careful and extensive trial of the various tuberculin reactions that the Pirquet test runs approximately parallel with the subcutaneous test, but neither is of value except in excluding tuberculosis when negative. The conjunctival test, on the other hand, is of most value when positive, the reaction indicating active tuberculosis. It is accordingly advisable to use the Pirquet test and the Calmette test simultaneously.

R. C. Rosenberger (*Am. J. M. Sc.*, Feb., 1909) announced early in the year that tuberculosis in any of its forms is a bacteriæmia, the bacilli being invariably demonstrable by mixing the blood with an equal volume of citrate solution, and examining the sediment after laking it with water. C. E. Forsyth (*Brit. M. J.*, April 24, 1909) later confirmed this observation, using practically the same method and finding the organisms in the blood of each of 12 cases of tuberculosis. Burnham and Lyons, however, found it impossible to demonstrate the bacilli in the blood in any of 10 cases

of undoubted tuberculosis; and Ravenel and Smith had the same experience with 18 cases. Schroeder and Cotton (*Arch. Int. Med.*, Aug., 1909) found no evidence of tubercle bacilli in the blood of tuberculous cattle, and suggested that the original method was faulty.

Bailey (*Boston M. and S. J.*, Sept. 2, 1909) attempted to confirm Rosenberg's results, but found acid-fast bodies only occasionally, and was utterly unable to produce tuberculosis in guinea-pigs by injecting the blood into them. He stated that the bacilli found by earlier observers might be artefacts or attenuated, non-virulent tubercle bacilli, or some sort of contamination introduced during the process.

W. V. Brem (*J. Am. M. Ass.*, Sept. 18, 1909), in a careful investigation of the matter, found that acid-fast micro-organisms can often be found, not only in the ordinary containers of water and other reagents, but even in such a location as the reservoir of a water-distilling apparatus when animals are kept in the same building.

W. A. Sawyer (*Arch. Int. Med.*, Dec., 1909) finds that tubercle bacilli introduced into the blood can be demonstrated much more easily by laking the blood and then centrifuging to sediment the bacteria than by sedimenting the whole blood and laking afterward. Even this method, however, only rarely gave positive results in obviously tuberculous cattle. Rosenberger still holds to his original views as to the value of the test, if the search for the bacilli is a very thorough one and is made by a competent bacteriologist.

E. Krencker (*München. med. Wchnschr.*, May 18, 1909) reports the typhoid agglutination reaction positive in 8 out of 26 cases of tuberculosis, and advises care in accepting a positive Widal test. All of the 8 cases had an elevated temperature.

A. Wolff-Eisner (*Med. Klin.*, June 13, 1909) emphasizes the advantage of the conjunctival reaction in differentiating active from quiescent tuberculosis. As the result of examining 4500 cases he finds that a very marked reaction indicates a good resistance on the part of the patient and allows a favorable prognosis, while a negative reaction in obvious tuberculosis means an unfavorable prognosis.

A. Bauer (*Beitr. z. Klin. d. Tuberk.*) points out the importance of enlargement of the supraclavicular group of lymphatic glands as an early sign of tuberculosis of the lungs.

G. Pollaci (*Riforma med.*, Aug. 9, 1909) advises a "lip test" instead of the conjunctival test for tuberculosis. The tuberculin is dropped on the mucous membrane between the lower teeth and the lip, the latter being held away from the jaw for a minute until the tuberculin is absorbed. The reaction is similar to that of the conjunctiva, but has the great advantage of freedom from the dangerous sequelæ that have been reported as following the ophthalmo-reaction, and at the same time appears to be more delicate.

G. E. Ebricht (*Am. J. M. Sc.*, Sept., 1909) finds it perfectly practicable to shorten the time required in using guinea-pigs for testing suspected tuberculous matter by using the tuberculin reaction in them a week after inoculation instead of making an autopsy after a month or more. The method has the advantage of simplicity, and positive reactions are conclusive. It furnishes a good method for discriminating between tubercle bacilli and other acid-fast forms which resemble them.

F. P. McCarthy (*Boston M. and S. J.*, Sept. 20, 1909) reports 263 cases in which ophthalmo-reaction was used. Failure to react was found in a few of the more advanced cases of tuberculosis, but the early stages were always positive. Several of the cases of typhoid fever gave a positive reaction, and one of the cases of malaria.

F. Malmejac (*Presse méd.*) states that in tuberculosis the urine is characterized by its lasting acidity, this often persisting for weeks and even months instead of disappearing after a few days' standing. The phenomenon is found in 97 per cent. of the cases and is often helpful in making an early diagnosis.

T. Sato (*Beitr. z. Klin. d. Tuberk.*) finds that the tuberculin test can be given *per os*, the febrile reaction corresponding exactly to that seen when hypodermic injections are used. One milligramme of old tuberculin is given in a capsule on an empty stomach. A positive reaction is conclusive, and is obtained in the great majority of cases of tuberculosis.

C. McNeil (*Brit. M. J.*, Nov. 6, 1909) finds the conjunctival

and cutaneous reactions of great value, especially in obscure joint affections such as slight continued impairment of function following injury. The conjunctival reaction was never found positive when the cutaneous reaction was negative.

C. Krämer (*Beitr. z. Klin. d. Tuberk.*) finds that an important early sign of tuberculosis is the dulness on percussion between the scapulæ due to affection of the bronchial lymphatic glands.

SYPHILIS.—Blumenthal and Roscher (*Med. Klin.*, Feb. 14, 1909) find that the Wassermann serum-reaction for syphilis is always negative during the first six or eight weeks of the disease. In an active secondary stage the reaction is always positive, but it becomes less strongly marked, or even absent, on vigorous mercurial treatment.

F. Lesser (*Deutsche med. Wchnschr.*, Mar. 4, 1909) reports 2000 cases of syphilis in which the Wassermann reaction was tried. All cases of progressive paralysis were positive, but only about one half of the cases of locomotor ataxia. He finds that unusually vigorous treatment is necessary to transform a positive reaction into a negative one, and it is rarely possible in alcoholics or in children with inherited syphilis.

R. Ledermann (*Med. Klin.*, Mar 21, 1909) reports 550 cases of the Wassermann reaction, and emphasizes its importance at health resorts where many patients come with a vague history and obscure symptoms.

C. Goosman (*J. Am. M. Ass.*, May 15, 1909) points out that elaborate accessory apparatus is not necessary for demonstrating the spirochæta of syphilis by dark ground illumination. He uses a series of home-made "stops," giving annular illumination, under a 1.20 N. A. condenser, and a high power dry objective. A little practice with a knowledge of the principles involved, makes the process no more difficult than the ordinary dark-ground illumination with a low magnifying power by means of stops.

H. Noguchi (*J. Exper. M.*, March, 1909) describes a modification of the serum-reaction for syphilis in which the hæmolysin, complement, and toxin are preserved dry in saturated slips of filter paper which may be kept indefinitely. The hæmolysin is produced by immunizing against human blood, so that the patient's blood contains not only the amboceptor of the syphilitic system but

the cell-substance of the hæmolytic system as well, and thus takes the place of the suspension of sheep corpuscles.

B. Sachs (*J. Am. M. Ass.*, Sept. 18, 1909) gives a detailed report of 28 cases of tabes with a positive serum reaction in 64 per cent., and 31 of general paresis with the reaction positive in 68 per cent.

H. Noguchi (*J. Am. M. Ass.*, 1909) gives tables summarizing the results obtained by the Wassermann and Noguchi tests in over 2000 cases. He points out the advantage of his own method in that there is always a known quantity of hæmolytic amboceptor, whereas in the Wassermann technic the human serum may contain considerable amounts of natural hæmolysin for sheep corpuscles. Other advantages are the convenient and stable form of the reagents, the small quantity of blood needed, and the fact that inactivation is unnecessary.

A. Reinhart (*München. med. Wchnschr.*, Oct. 12, 1909) reports 1600 cases in which the Wassermann test was used. It was almost uniformly negative in cerebral syphilis, but invariably positive in syphilitic bone lesions. It was more often positive in general paralysis than in other late syphilitic manifestations, and in early tabes than in the more advanced cases.

TYPHOID FEVER.—F. S. Hammond (*J. Am. M. Ass.*, Jan. 2, 1909) reports the case of a typhoid "carrier," with a complicating tuberculosis, in which enormous numbers of typhoid bacilli were found *post mortem* in the gall-bladder and liver, although a systematic course of hexamethylenamine had been given for many months.

Proescher and Roddy (*J. Am. M. Ass.*, Feb. 6, 1909) report 48 cases of paratyphoid fever, from which they conclude that paratyphoid differs from true typhoid in being due to a different bacillus, coming on more suddenly, lasting a shorter time, and being milder than typhoid. The temperature is never extremely high, complications are rare, sequelæ are absent, and the mortality is less than 2 per cent.

Graham, Overlander, Overlander, and Dailey (*Boston M. and S. J.*, Jan. 14, 1909) report a series of 65 typhoid cases in which the bacilli were found in the urine and stools ten days after discharge from the hospital. They urge detention of all typhoid

patients on recovery, and supervision by the boards of health as long as any of them remain carriers of the bacilli.

S. J. Deehan (*Univ. Penn. M. Bull.*, Aug., 1909) considers the typhoid cutaneous reaction a valuable one, and one which is easily applied and perfectly free from danger or discomfort. It was positive in every case of typhoid which he tested and negative in the other diseases.

W. Gähtens (*Deutsche med. Wchnschr.*, Aug. 5, 1909) finds that the opsonic index remains permanently high in typhoid patients who become bacillus carriers, while after a normal recovery it falls after a few months.

A. J. Brown (*J. Am. M. Ass.*, Feb. 27, 1909) calls attention to two new signs of perforation in typhoid fever. One is a crackling sound on placing the bell of the stethoscope over the right iliac fossa and pressing it down suddenly as in "dipping" palpation. The sound resembles a fine crepitant râle, as if two sticky inflamed surfaces were brought into contact and then separated. The other sign is an area of tenderness on pressure which tends to move toward the lower side when the patient is turned first on one side and then on the other.

W. Loele (*Deutsche med. Wchnschr.*, Aug. 19, 1909) describes a case of a typhoid carrier with cholelithiasis who was operated upon three months after the typhoid fever. The gall-bladder was found to be free from micro-organisms, so that cholecystectomy in this case would not have influenced the focus of proliferation of the bacilli.

Jopson and Gittings (*Am. J. M. Sc.*, Nov., 1909) report that typhoid in children, according to all the available statistics (4947 cases) results in perforation in 2.19 per cent., being very rare before 5 years of age, but after this becoming about half as frequent as in adults. The most probable period in the disease is during the third week. The diagnostic signs, in order of importance, are pain, tenderness, rigidity, fall in temperature, rapid pulse with collapse, vomiting, chill, and increasing leucocytosis. The mortality is lower than in adults; less than 50 per cent.

DIPHTHERIA.—M. Solis-Cohen (*J. Am. M. Ass.*, Jan. 9, 1909) reports 130 cases of diphtheria "carriers," apparently healthy persons whose throats contained the Klebs-Loeffler bacillus. He

points out that such cases may easily arise from chance contact with diphtheria patients, and that the bacilli in these cases are usually virulent and may later cause true diphtheria in the "carrier" himself or may be transferred to other persons. Disinfection of premises is of little use unless the individuals on the premises are disinfected as well, and they should be isolated, as long as they are found to remain possible sources of danger.

J. W. Fisher (*J. Am. M. Ass.*, Feb. 6, 1909) reports a diphtheria epidemic in an institution, in which there were 92 cases, and 95 other persons whose throats showed the presence of the bacilli. He finds that at least 4 successively negative cultures are necessary before positively excluding the presence of diphtheria. Two of these should be from the nasal mucous membrane. He advocates the isolation of "carriers" in institutional outbreaks but declares that in private practice it is neither reasonable nor expedient. They were found to retain the bacilli longer than did the patients with clinical diphtheria. During the epidemic 2.08 per cent. of the normal persons were carriers. Under ordinary conditions non-virulent diphtheria bacilli were found in the throats of 1.1 per cent. of healthy individuals.

D. H. Ransom (*J. Am. M. Ass.*, Feb. 13, 1909) reports a birth shortly after giving the mother 7000 units of antitoxin. The child remained perfectly well without further treatment although the mother and two other children were diphtheritic.

MENINGITIS.—H. Vincent (*Bull. Acad. de méd.*, Mar. 16, 1909) finds that the cerebrospinal fluid from meningitic patients gives a precipitin reaction when added to an agglutinating immune serum. If 1 drop is added to 50 or 100 of serum the mixture becomes turbid in 8 to 12 hours in all of the meningococcus cases, while it remains clear in cases of other disease or of healthy individuals.

Elser and Huntoon (*J. Med. Research*, June, 1909) describe the meningococcus, its relation to similar organisms, its identification and its biological reactions. They conclude that it is transmitted only by direct contact, and in epidemics there are usually more carriers than clinical cases of meningitis. The meningococcus probably lodges in the respiratory tract and is then conveyed by the blood to the meninges.

J. Brudzinski (*Arch. de méd. de enf.*, Oct., 1909) reports a new sign of meningitis which he finds to occur almost universally in meningitis and to be absent in all other conditions, being even more constant than Kernig's sign: passive flexion of the neck produces movements of flexion in the hip, knee, and ankle. He found the sign once in a case of pneumonia, but this soon developed into a pneumococcic meningitis with the pneumococci demonstrable in the spinal fluid.

POLIOMYELITIS.—Flexner and Lewis (*J. Am. M. Ass.*, Nov. 13, 1909) have recently succeeded in producing acute anterior poliomyelitis experimentally by inoculating monkeys with material from the spinal cord of cases in human beings and have demonstrated that the disease is a distinct infectious process. Tissue from the spinal cord was emulsified with salt solution and injected into the brain, under anæsthesia, after trephining. That this was not merely a transfer of toxic material was shown by passing the disease through 5 successive monkeys, the lesions produced in the anterior horns being similar to those found in human beings. Tissue from the cerebral cortex was likewise found capable of transferring the infection.

Later (*J. Am. M. Ass.*, Dec. 4, 1909) they report equal success with infectious material from a different case of acute anterior poliomyelitis, so that transmission to monkeys cannot be a very difficult matter. They find that intravascular, intraneural, and intraperitoneal injections will also convey the infectious process to its customary site of manifestation. A sciatic nerve inoculation resulted in the pathological process first appearing in the same side of the cord and later spreading to the opposite side. The experimental disease is severe and often fatal; recovery is accompanied by the same paralysis as in human beings.

They report further (*J. Am. M. Ass.*, Dec. 18, 1909) that the virus of poliomyelitis, like that of vaccinia and rabies is resistant to glycerin, and preserved its activity after being kept in that medium 7 days, producing the same disease, from which further successful inoculations could be made. It is apparently an ultramicroscopic organism, and can be passed through a Berkefeld filter. Subcutaneous infection has also been accomplished.

Le G. Kerr (*Long Island M. J.*, Nov., 1909) reports 53 cases of

acute anterior poliomyelitis in an epidemic. The chief symptoms, in order of importance, were fever, diarrhoea, cough, and vomiting.

INFLUENZA.—W. S. Harpole (*Chicago Med. Recorder*, Jan., 1909) concludes that Pfeiffer's bacillus often occurs in the throat or sputum in fevers or respiratory affections, and these may or may not be cases of mild influenza. It also occurs in whooping cough, scarlatina, measles, etc., as well as in perfectly healthy individuals, and is probably always present in the community but takes on a pernicious activity only at certain unknown times and places, from which it spreads rapidly, producing a pandemic.

H. Curschmann (*München. med. Wchnschr.*, Feb. 23, 1909) has demonstrated the pneumococcus in 49 cases of apparently typical influenza, while Pfeiffer's bacillus was never found in any of them.

MEASLES.—J. Ewing (*Jour. Infect. Diseases*, Feb., 1909) describes the essential lesions of measles as focal necrosis with vesicle formation, isolated necrosis of epithelial cells, diffuse cytoplasmic vacuolation, congestion, œdema and proliferation of epithelial cells, and an increase in the number of large round cells. There is a round cell infiltration of the respiratory mucosa, together with focal necroses, thus probably producing Koplik's spots. These changes suggest that the causal agent is a plant parasite rather than a protozoan one.

Hecker (*München. med. Wchnschr.*, Oct. 12, 1909) points out that there is a marked leucopænia as an early sign of measles. Usually it occurs a few days before Koplik's spots appear, but it may precede them by nearly 2 weeks.

Bieler (*Arch. de méd. d. enf.*, Oct., 1909) states that kidney affections in measles occur more commonly than is generally supposed. Pyelitis or pyelonephritis were found in 9 out of 147 cases and albuminuria in 59 others.

LEPROSY.—M. T. Clegg (*Philippine J. Sc.*, April, 1909) describes a series of experiments in growing the bacillus of lepra on artificial media. As it is found so frequently within cells the cultures were all made with an attempt at symbiosis, amœbæ being grown on agar with suitable symbiotic bacteria, and later leprosy bacilli being added instead of more of the original bacteria. After incubation many typical bacilli of leprosy were found, to-

gether with a short, thick bacillus which was also acid-fast, and as it was not found in controls, is probably to be considered the form which *Bacillus lepræ* assumes on being cultivated under these conditions. Transfers to fresh agar plates containing amœbæ showed conclusively that this organism was growing and increasing in numbers.

ROCKY MOUNTAIN SPOTTED FEVER.—H. T. Ricketts (*J. Am. M. Ass.*, Jan. 30, 1909) states that the ticks which transmit spotted fever may pass the infection onward to their young by means of the eggs, and reports the results of work done in investigating infected eggs of *Dermacentor*. When crushed, fixed in absolute alcohol, and stained with Giemsa's stain these were found to contain a great number of organisms about the size of the influenza bacillus and showing a bipolar staining affinity. Although eggs of ticks positively known to be free from spotted fever were not obtained, an examination of the viscera of both normal and infected ticks showed multitudes of similar structures in the salivary glands, alimentary sac, and ovaries of the latter, while none were to be found in those of the former.

Agglutination tests with these micro-organisms showed that normal guinea-pig's serum had no effect in 1:1 dilution or weaker. Complete agglutination was produced by immune guinea-pig's serum in dilutions of from 1:1 to 1:160, and partial agglutination with even higher dilutions. By adding immune serum to the fresh serum of an infected animal and centrifuging, the same organisms were demonstrable. They appear to be an exception to the rule that parasites having an arthropod as an obligate intermediate host are always protozoan in character.

MUMPS.—J. G. Sharp (*Lancet*, Jan. 16, 1909) emphasizes the importance of mumps and the comparative frequency with which the pancreas is affected. The abdominal symptoms, localized in the pancreatic region, may be the first sign of the disease, or they may appear only after a long period following the parotitis. They may appear very suddenly and pass away with equal rapidity. The relatively slow pulse and low temperature are helpful in differentiating such cases from peritonitis.

I. C. Herb (*Arch. Int. Med.*, Sept., 1909) reports the isolation of a diplococcus from a case of mumps, describing its growth

and characteristics. It causes a diffuse, non-suppurative parotitis when injected into Steno's duct in dogs and monkeys, and in the single case of human mumps which was studied there was a rise in the opsonic index for this organism. The micro-organism corresponds well with the one described by Laveran and Catrin from cases of parotitis.

DYSENTERY.—Metchnikoff (*Bull. Acad. d. Med.*, Nov. 23, 1909) finds that the *Bacillus proteus* will produce a characteristic "summer diarrhoea" in monkeys, and is undoubtedly the cause of the same affection in children. It is abundant in the dejecta of various domestic animals and probably carried by flies to the child's food. It is easily killed by drying, boiling, etc.

CONSTITUTIONAL DISEASES

PELLAGRA.—Since pellagra was first recognized in Alabama and South Carolina in 1907 it has continually increased in importance and interest in the South, and in the United States generally. Most of the cases have been in the South Atlantic and Gulf States, and in Illinois. The importance of a diet of Indian corn in the etiology of the disease, and its prevalence among the poorer classes have been very evident. There is an increasing belief in the probability of some mould, as *Penicillium glaucum*, or some sporozoön, as the etiological factor.

J. H. Randolph (*Arch. Int. Med.*, Jan., 1909) states that negroes are less susceptible than white persons, but the disease attacks both sexes with equal frequency.

N. P. Walker (*J. Am. M. Ass.*, July 3, 1909) describes pellagra as seen in 51 cases in a Georgia institution. The age varied from 6 to 75 years. Colored persons seemed more often affected than whites, and women more often than men. The dermatitis, stomatitis, and diarrhoea usually appeared simultaneously. Nucleated red corpuscles were found early in the disease even when the hæmoglobin was normal or high.

E. J. Wood (*J. Am. M. Ass.*, July 24, 1909) discusses the disease in detail as described in the reports of 200 American cases which he has collected, and reports 6 more cases; 4 chronic, and 2 acute.

L. J. Pollock (*J. Am. M. Ass.*, Oct. 2, 1909) reports 14 cases

and emphasizes the facts pointed out by Babcock (*J. South Carolina Med. Ass.*, Nov., 1908) of the high mortality, large number of women affected, and wide-spread areas of dermatitis, in the cases seen in the United States.

C. C. Bass (*J. Am. M. Ass.*, Oct. 9, 1909) finds that the Wassermann test, using lecithin as antigen, is markedly positive in cases of pellagra. This is additional evidence in favor of the disease being due to some protozoan organism.

DIABETES.—W. Ebstein (*Deutsches Arch. f. kl. Med.*, 1909, xcv, 1) states that there is a close relationship between diabetes mellitus and diabetes insipidus. The latter is very rare in elderly people, the symptoms of it being more often due to contracted kidney, even if tube-casts and albumin are absent from the urine. Diabetes insipidus usually has a nervous origin, and the cases developing after syphilis are probably due to the action of the syphilitic virus on the nervous system, the pathological change being in the medulla.

James Tyson (*Univ. Penn. M. Bull.*, Jan., 1909) discusses the acidosis of diabetes and emphasizes the importance of allowing sufficient carbohydrate in the diet. He gives the following test for acetone: 1 cubic centimetre of acetic acid and one drop of strong nitro-prusside solution are mixed with the urine, which is then overlaid with ammonia. A beautiful purple color is formed at the surface of contact if acetone is present.

H. Busquet (*Presse méd.*, Jan. 9, 1909) finds that the sugar excretion of diabetic patients is increased on exposure to cold and decreases when they are kept in a well-warmed room.

F. Hirschfeld (*Deutsche med. Wchnschr.*, Jan. 28, 1909) emphasizes the importance of infectious processes in causing diabetes. The chronic pancreatitis of diabetics has generally resulted from acute or subacute infectious inflammations previously, the process being similar to cirrhosis in the liver. The pancreas and liver are often affected simultaneously, but if the liver has been previously injured, as by alcohol or malaria, it shows the greater degree of change and the pancreatic process then rarely progresses far enough to cause diabetes.

H. Senator (*Zeits. f. kl. Med.*) finds that the glychæmia of rabbits is much increased when they are kept at a high tem-

perature. The urine may be free from sugar, however, even if the blood contains as much as 2.8 parts per thousand.

A. P. Mathews (*J. Biol. Chem.*, Mar., 1909) finds that the oxidation of sugar takes place more rapidly in a weak alkaline solution, this causing a preliminary ionization of the sugar. Some similar process probably occurs in the living organism, some substance being present which unites with the sugar and renders it more dissociable. He suggests the term *metabolases* for such substances, which very likely also produce metabolic changes other than the oxidation of sugar.

H. Citron (*Deutsche med. Wchnschr.*, July 18, 1909) describes an advantageous test for sugar estimation by heating with an excess of Fehling's solution, liberating iodine from iodide and acid by the copper remaining in solution, and then titrating the iodine with thiosulphate and starch solution.

H. R. Harrower (*Med. Rec.*, Aug. 28, 1909) describes a method of estimating ammonia in the urine with oxalic acid, sodium hydroxide solution, formaldehyde, and phenolphthalein in a specially graduated glass tube.

R. W. King (*J. Am. M. Ass.*, Nov. 20, 1909) describes an inexpensive apparatus by which the ammonia and acetone of the urine can be easily estimated with accuracy.

E. W. Brown (*J. Am. M. Ass.*, Dec. 18, 1909) discusses the formaldehyde method of estimating urinary ammonia, titration with sodium hydroxide liberating ammonia, which forms hexamethylenamine with the formaldehyde, while the sodium hydroxide replaces it in the neutral salts until an excess is present. He finds that clearing the urine with lead subacetate before adding potassium oxalate makes the end reaction with phenolphthalein very much sharper and at the same time increases the accuracy of the method. The technic of the test, which is rapid and simple, is given in detail.

OBESITY.—Von Noorden (*Med. Klin.*, Jan. 3, 1909) states that there are two distinct forms of obesity, one in which there is disproportion between exercise and ingestion of food, and another which is due to the influence of the thyroid gland on metabolism. The hypothyroidism may be primary or it may be due to some

abnormal function of other ductless glands, such as the pancreas, ovaries, pituitary, suprarenals, or thymus. He discusses the corresponding indications for treatment.

F. H. Church (*J. Am. M. Ass.*, Oct. 2, 1909) advises determining whether a red color in performing the Jaffé test is due to indigo red or to iodine by removing the chloroform and testing with alkali and starch solution. He states that Gerhardt's test for diacetic acid may be made much more satisfactory by adding the urine drop by drop to 10 or 15 cubic centimetres of the dilute iron solution.

DISEASES OF THE DIGESTIVE ORGANS

H. Finklestein (*Deutsche med. Wchnschr.*, Feb. 4, 1909) states that an alimentary fever is possible from the ingestion of food alone. The proteid of the food is not responsible for it, but it is produced by crystalloids, such as sugar or salts, which have an injurious influence on the cells and cause a perverted metabolism in cases where gastro-intestinal disturbances are present, resulting in the production of fever.

L. F. Meyer (*Deutsche med. Wchnschr.*, Feb. 4, 1909) corroborates Finklestein's work and finds that the salts responsible for alimentary intoxication and fever are limited to the halides of sodium, or, in practically all cases, sodium chloride.

W. Krienitz (*Arch. f. Verdauungs Krankheiten*) finds that the Cammidge reaction is positive in about 80 per cent. of the cases of pancreatic disease, and is very useful as an aid in diagnosis.

A. E. Austin (*J. Med. Research*, Feb., 1909) finds that enterokinase is not present in children before 24 days of age, but after that time, is present in a certain number of them.

Eichler and Schirokeuer (*Berl. klin. Wchnschr.*, Feb. 15, 1909) find that the Cammidge reaction is only occasionally positive in dogs with experimental pancreatitis. It was found negative in two cases in which later operation showed fat necrosis and chronic indurative pancreatitis. They consider that the reaction is of comparatively little value.

O. Füller (*Deutsche Zt. f. Chirurgie*, Feb., 1909) finds that Rovsing's sign is not a very reliable indication of appendicitis.

Pain at McBurney's point was produced by pressure on a spot symmetrically situated on the left side in one case of renal sarcoma, and could not be produced in about four fifths of the cases in which appendicitis was present.

O. Schwarz (*Wien. klin. Wchnschr.*, Mar. 4, 1909) finds Sahli's glutoid test, Schlecht's trypsin test, and Cammidge's pancreatic test all of value in diagnosing pancreatic affections, the Cammidge reaction being particularly reliable. It is almost invariably positive in cases of a circumscribed pancreatic tumor, and becomes negative after successful operative removal.

M. Einhorn (*Med. Rec.*, April 3, 1909) describes a method of locating peptic ulcers by having the patient swallow at night a 'bucket' enclosed in a gelatin capsule and attached to a silk thread 75 centimetres long. This is withdrawn the next morning and the silk will be found stained with blood at a distance from its end corresponding to the location of the ulcer. He describes another method, in case of gastric ulcer, by using a rubber balloon covered with silk gauze and shaped like the stomach. This is attached to a rubber tube, by which it is inflated after being swallowed.

F. P. Kinnicutt (*Med. Rec.*, April 10, 1909) gives a summary of 51 cases of suspected pancreatic disease in which the Cammidge reaction was tried. He concludes that it is not pathognomonic, but yet is strongly suggestive of pancreatic inflammation or tissue destruction, and is a valuable aid to the diagnosis of pancreatic disease.

E. P. Fick (*J. Am. M. Ass.*, April 3, 1909) describes a simplified method and apparatus for determining gastric acidity. A glass tube is used which holds 25 cubic centimetres and is graduated in tenths of a cubic centimetre. The indicator is put in it, together with enough gastric juice to fill it to the 10 c.c. mark, and then the decinormal alkali is added in small amounts, the tube being corked and shaken after each addition. Standard tubes are used to furnish a color for comparison to indicate when the end reaction is reached.

S. Livierato (*Gaz. d. osp.*, Mar. 18, 1909) finds that the gastric juice of patients with gastric cancer will fix complement when

cancer extract is added. The inhibition of hæmolysis produced in this manner is used as a clinical test, being positive in the 8 cases of undoubted cancer of the stomach in which it was tried and negative in all persons free from cancer.

J. S. Hall (*Am. J. M. Sc.*, May, 1909) finds that in 50 consecutive cases of peptic ulcer, in which the diagnosis was proved by operation, pain was present in 82 per cent., hyperacidity in 80 per cent., tenderness in 70 per cent., vomiting in 66 per cent., and rigidity in 60 per cent. Gastric hemorrhage was found in only 34 per cent., and blood in the stools in only 8 per cent. Cases with dilatation and permanent loss of motility generally fail to improve. Enlarged lymph-glands are frequently found on operation and should not lead to a mistaken diagnosis of carcinoma.

O. Gross (*Deutsche med. Wchnschr.*, April 22, 1909) reports 200 cases of examination of the stools by the casein test for trypsin, the undigested part of the casein alone being precipitable by acid. Trypsin was found in the stools in all cases of normal digestion, but was constantly wanting in a case of pancreatic cancer and in a case of complete stoppage of the common bile-duct.

G. H. Wright (*Boston M. and S. J.*, May 20, 1909) emphasizes the importance of the condition of the teeth, in causing tonsillar inflammation, the infectious agents being carried by way of the neighboring lymphatics.

H. Kehr (*München. med. Wchnschr.*, May 25, 1909) reports 58 cases of gall-stones where the symptoms suggested secondary pancreatic trouble. The Cammidge test was confirmed in 20 out of the 22 cases in which an operation was performed. He thinks that it may be more reliable in chronic pancreatitis than in acute cases, as it was constantly negative in a case of sudden, acute necrosis.

M. E. Rehfuß (*Univ. Penn. M. Bull.*, June, 1909) from experimental work in the production of gastric ulcer, finds that the most important factor is systemic intoxication, the kind of poison being of comparatively little importance provided that it is given in amounts large enough to produce marked toxic symptoms. The ingestion of alkaline fluids inhibits ulceration and in most cases prevents it, so that the digestive action of the gastric juice would

appear to be the primary factor in producing the condition, which seems to be due to local malnutrition brought about by stagnation of the circulation.

Berger and Tsuchiya (*Deutsches Arch. f. kl. Med.*, 1909, xcvi, 252) find that an extract from the gastro-intestinal mucous membrane in certain pathological conditions has a marked hæmolytic action, and conclude that inflammatory gastro-intestinal infiltration is important in the development of pernicious anæmia. Inflammatory catarrh causes the development of a strongly hæmolytic substance of a lipid nature, but the hæmopoietic organs show a compensatory activity, and pernicious anæmia results only if the process is a very severe or long-continued one.

Guiart and Garin (*Semaine méd.*, Sept. 1, 1909) find that trichocephalus infection invariably cause the guaiac test for blood in the stools to be positive, care being taken to rule out possible complications from a meat diet. Accordingly, a positive test for occult blood should never be taken as confirming a diagnosis of cancer unless examination of the stools shows that this parasite is absent. *Ascaris* also causes the same results, but not as constantly as trichocephalus.

J. E. Schmidt (*Mitt. a. d. Grenzgeb. d. Med. u. Chir.*) concludes from clinical evidence and experimental work on cats and dogs that a positive Cammidge reaction where pancreatic trouble is suspected is of great corroborative value, as the reaction is positive chiefly in diseases in which there is much destruction of glyconucleoproteids, such as pneumonia or appendicitis with diffuse peritonitis, and these are not likely to be confused with pancreatic disease.

A. Müller (*Med. Klin.*, Sept. 19, 1909) finds that gastric acidity may be simply and easily estimated by adding tropæolin 00 to gastric juice in the proportion of 1 to 50 and comparing the mixture with a color scale previously standardized. In 24 cases in which it was tried this test agreed closely with the more complicated ones in general use.

E. H. Goodman (*J. Am. M. Ass.*, Dec. 18, 1909) finds alimentary levulosuria almost constantly present in cases of hepatic cirrhosis, the prompt or tardy appearance of the sugar in the urine

corresponding to a severe or a mild case respectively. Although it does not indicate any specific hepatic lesion, it is most frequently observed in cirrhosis and is an important aid in distinguishing this condition from chronic passive congestion.

RESPIRATORY DISEASES

F. M. Pottenger (*J. Am. M. Ass.*, Mar. 6, 1909) states that rigidity of the muscles of the chest wall, particularly of the intercostals, is a useful sign of diseases of the lungs as well as of those of the pleura. Gentle pressure with the finger tips over the interspaces gives a sensation similar to the familiar feeling of abdominal rigidity.

H. Sewall (*Am. J. M. Sc.*, Mar., 1909) reports a case which shows undoubtedly that the "new-leather sound" as well as the dry friction rub may be present when there is no reason whatever for suspecting pleural friction. He considers that it must be due to intrapulmonary rubbing of the tissues during respiration.

Pottenger (*Am. J. M. Sc.*, May, 1909) finds that the intercostal rigidity described previously is a constant sign in pulmonary tuberculosis, it being possible to mark out the affected areas by the location of the rigidity, and to judge the severity of the process to a certain extent by the degree of tenseness. The sign is absent in areas where superficial cavity formation occurs.

F. Semon (*Brit. M. J.*, June 26, 1909) reports a case of pneumococcus invasion of the throat, two cases having been previously described. Areas of infiltration and of ulceration were present, the latter showing almost a pure culture of pneumococcus. Edema of the larynx and other complications caused death after about the seventh month.

KIDNEY DISEASES

J. T. Geraghty (*Johns Hopkins Hosp. Bull.*, Jan., 1909) finds that persistent bacteriuria is always due to micro-organisms of slight pathogenicity, and depends upon some focus of infection in or near the urinary tract. It may last indefinitely in spite of treatment without producing any inflammatory reactions in the mucosa of the bladder. When due to the colon bacillus the urine

is acid; when due to *Staphylococcus albus* it may be alkaline and give rise to a troublesome phosphaturia.

O. Klotz (*J. Med. Research*, Jan., 1909) finds that the so-called large white kidney contains sodium and potassium compounds of oleic acid, and suggests that the name *soapy kidney* would be more appropriate than the more usual one of fatty kidney.

Torday and Klier (*Deutsche med. Wchnschr.*, Aug. 20, 1909) state that a red coloration produced by methyl violet, discovered by accident, is a most delicate test for bile pigments, and will show bile in the urine in such small amounts that all the other commonly used tests are negative.

DISEASES OF THE BLOOD

W. Whittemore (*Boston M. and S. J.*, Jan 21, 1909) concludes, from the study of over 100 cases, that hæmolysis is of practically no value in determining the presence of carcinoma. It was present in 36 per cent. of the cases of this condition; 17 per cent. of normal persons; 50 per cent. of the cases of tuberculosis; and in various other conditions, such as Hodgkin's disease, empyema, tabes, malaria, etc.

L. Heim (*München. med. Wchnschr.*, Jan. 5, 1909) finds that the sources of immune sera have not been nearly utilized as yet, it being perfectly possible and practicable to obtain immune bodies from the fixed tissues, especially muscle substance, which contains them in large amounts.

R. S. Morris (*Arch. Int. Med.*, Mar., 1909) reports the presence of nuclear particles in the red blood-corpuscles as an important evidence of the regeneration of the blood in various conditions in which it has become impoverished, and describes the technic of staining them.

O. Thomsen (*Hospitalstidende*, Feb. 17, 1909) reports experimental work which shows that the phenomenon of anaphylaxis can very well be made use of in forensic tests of blood stains. The small amount of specific proteid in an extract of the blood stain is enough to produce in a guinea-pig a condition of hypersensitiveness toward the blood-serum of the species from which it was derived.

F. Hesse (*Deutsche med. Wchnschr.*, Aug. 12, 1909) points out the importance of retinal hemorrhages as a differential sign of

pernicious anæmia. They occurred in 47 out of 50 cases, but were entirely absent in 64 cases of carcinoma, 29 of them being gastric cases, as well as in 51 cases of severe secondary anæmia from other causes.

CIRCULATORY DISEASES

J. A. Hartwell (*J. Am. M. Ass.*, Jan. 23, 1909) describes a simple method for transfusing blood without a canula. The artery and vein of donor and receptor respectively are dissected out, clamped, and cut, and the adventitia is removed except for a small strip some distance back from the cut end of the artery. Three sutures are put in the cut end of the vein. The end of the artery is then treated with melted petrolatum to avoid any chance of causing coagulation and inserted into the cut end of the vein for a distance of about an inch, the sutures of the vein being tied to the adventitia of the artery and any loose circumference of the vein being caught up with a clamp. The blood will now flow freely from artery to vein when the clamps are removed without leaking back around the artery.

Ehret (*München. med. Wchnschr.*, Mar. 25, 1909) finds that a simple method of determining the diastolic blood-pressure with accuracy is by palpating the artery just beyond the distal edge of the cuff of the ordinary sphygmomanometer. A sudden change in the strength of the pulse is felt when the pressure in the manometer corresponds to the diastolic pressure in the artery.

M. Landolfi (*Semaine Méd.*, July 28, 1909) states that in uncomplicated aortic insufficiency there is sometimes a true hippus synchronous with the contraction and dilation of the heart. It is found only in cases with good compensation.

M. Roch (*Rev. de Méd.*, Aug., 1909) has observed the same phenomenon, and also a hippus synchronous with the respiratory movements of the chest.

H. Engel (*Berliner klin. Wchnschr.*, Sept. 20, 1909) points out the importance of a constantly continued difference in blood-pressure in two separate locations as a sign of arteriosclerosis, even though the difference amounts to only a few millimetres of mercury. The phenomenon is due to some localized angiosclerotic change and is accordingly useful in differentiating conditions primarily renal in origin from those primarily vascular.

NERVOUS DISEASES

A. J. Rosanoff (*J. Am. M. Ass.*, Feb. 13, 1909) tabulates a large number of mental and nervous cases, and shows that there is a striking immunity to tuberculosis in cases of general paresis, this being independent of the fact that the age of incidence of general paresis is greater than that of greatest susceptibility to tuberculosis. As paretics are immune to syphilis it is suggested that it is the syphilitic virus which causes their immunity to tuberculosis as well.

Ross and Jones (*Brit. M. J.*, May 8, 1909) describe two new tests for determining the excess of globulin in the cerebrospinal fluid which is characteristic of parasyphilitic affections. One consists of the addition of 5 volumes of 10 per cent. pure butyric acid solution and one volume of 4 per cent. sodium hydroxide and heating. A flocculent precipitate occurs instead of a mere opalescence. The other is a positive ring test within 3 minutes after underlaying with a saturated solution of ammonium sulphate as in Heller's nitric acid test for albumin.

Much and Holzmann (*Münchener med. Wchnschr.*, May 18, 1909) find that the blood-serum of patients with dementia precox or manic depressive insanity inhibits the hæmolysis caused by cobra venom. Examination of 400 specimens of serum showed the reaction positive in cases of these diseases and of patients whose parents had had either of these conditions; in all others it was negative. The "psycho-reaction" is given only by the serum, not by cerebrospinal fluid, and is important in diagnosis and in forensic medicine, as well as from a theoretical point of view.

Hübner and Selter (*Deutsche med. Wchnschr.*, July 18, 1909) find the Much-Holzmann reaction positive in less than half the cases of manic depressive insanity and dementia precox and report a positive reaction in several other neuroses, psychoses, and organic nervous affections.

F. Bauer (*Münchener med. Wchnschr.*, July 6, 1909) finds the psycho-reaction of Much and Holzmann positive in 14 out of 17 cases in which the blood from the umbilical cord in new-born infants was examined. The blood of 25 other children was uniformly negative.

Hirschl and Pötzl confirm the results of Much and Holzmann in 50 cases of dementia precox of the catatonic and hebephrenic forms.

A. J. Rosanoff (*Arch. Int. Med.*, Oct., 1909) finds that the psycho-reaction is not pathognomonic of any particular psychosis but occurs more frequently in dementia precox than in any other condition. In 15 typical cases of manic depressive insanity the reaction was uniformly negative.

J. Larat (*Presse méd.*, Dec. 8, 1909) finds that a reaction characteristic of traumatic neuroses is an anodal closing contraction which is greater than the cathodal closing contraction, but showing a sharp "peak" in the graphic record instead of the gradually rounded summit seen in the slow contraction of obvious degeneration.

SURGERY

BY JOS. C. BLOODGOOD, M.D.

POSTOPERATIVE COMPLICATIONS

IN considering these complications it is best, first, to discuss the preparation for operation and the postoperative measures which have for their object either to prevent them entirely, or to reduce their dangers. The subject of preparation for anæsthesia and operation is a very important one, but one finds very little on this subject in literature. In the hands of many surgeons this preparation varies, but there are certain procedures that appear common to all. Each year surgeons are impressed with the importance of presenting to the patient and to the family necessary surgical intervention in a manner that will reduce and perhaps eliminate the elements of fear and anxiety. Before any operation, the bowels should be freely moved. For all operations upon the abdomen, and especially those in which a hollow viscus is attacked, the intestinal canal should be thoroughly evacuated at least forty-eight hours before operation, and the patient should be placed upon a diet consisting of water and white of egg.

There is a great deal of surgery to be done, and as surgeons get busier and are required to do more and more operations each day, they find it more and more difficult to impress upon those assisting them in their work the great importance of the preparation of patients for operation. Without any particular care hundreds, perhaps, are subjected to operation without any complications, and yet, the few who have been most carefully prepared, may become victims of such complications.

I am impressed, however, with the fact that, as experience increases, the importance of a routine preparation will take a more prominent place in the surgeon's mind. Every patient should have at least the permissible minimum of preparation; should be subjected to a thorough examination, and, in the presence of

certain organic lesions, the maximum amount of preparation should be given in this selected group.

The minimum preparation for all the normal patients and the maximum for the smaller abnormal group accomplish the end in view with the least amount of labor to all concerned in the surgery of the day. One, however, must insist upon unusual vigilance in the study of the cases, and patients must not be rushed to the operating room for apparently simple lesions without most careful supervision. I write this advisedly, but I am confident, from my own observations, that in a country like ours, where small hospitals are springing up with great rapidity and a great deal of surgery is being done by an as yet inexperienced clinic, that a warning of this kind should be constantly sounded. If in the larger and older clinics eternal vigilance is required to accomplish the proper examination and preparation before operation, the same care will be required in the younger and smaller clinics.

Space forbids details, but I would urge upon surgeons to study carefully, first, what may be called the psychotherapy, consisting in the proper presentation of the operation, its necessity, and the prognosis to the patient. Second, the study of the cathartics, the enema, and the food. There is no reason why the preparation should cause discomfort. Without care in detail, one will find that one's patients are given great annoyance by excessive catharsis. The starvation diet may be carried too far. It is very difficult to impress upon the nursing staff and the patient the importance of plenty of water.

The subject of anæsthesia I will discuss later, but it must be decided whether the patient shall be placed on the operating table, the field of operation prepared, and then the anæsthetic given, or whether narcosis shall begin in a special room. There seems to be great difference of opinion on this question. I have had a large experience with both methods, and, except in selected cases, prefer the former. I am quite certain that, with the majority of people it creates less fear or anxiety; in all it reduces the quantity of anæsthetic required.

During the operation postoperative complications can in a measure be prevented or lessened by good anæsthesia and a wound technic which reduces the loss of blood and injury to tissues to

a minimum. During the operation it is of the greatest importance that the patient be kept dry and at a proper temperature.

After operation, there are two procedures on which the majority of American surgeons agree: the Fowler position and proctolysis. Cole¹ has summarized the views of fifty leading American surgeons upon this subject.

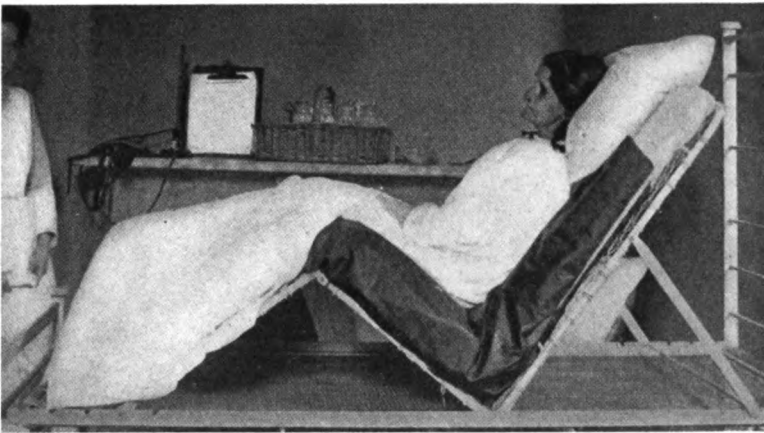
THE GATCH BED.—I have now had sufficient experience with the bed devised by Willis D. Gatch, assistant resident surgeon in the Johns Hopkins Hospital, to recommend it. Figs. 1 and 2, from *Annals of Surgery*, 1909, vol. xlix, p. 410, show the bed and sitting position. This folding bed can be placed on any hospital bed, and on it the ordinary mattress is most comfortable.

PROCTOLYSIS.—The method of giving salt continuously per rectum is now so well known that it almost seems unnecessary to mention it in a review on surgery. But I look upon it as one of the most important of the postoperative therapeutic procedures. In recent literature there are a number of contributions describing new apparatus for proctolysis. I should like to call attention to the one devised by Peregrine Wroth.² This apparatus was gotten up by him while he was resident surgeon of the Union Protestant Hospital in Baltimore. If one will examine Fig. 3 it will be unnecessary to take space for a description.

EARLY RISING OF PATIENTS AFTER OPERATION.—As to the time an individual should stay in bed after an operation, there is still a great difference of opinion. The older view that a patient subjected to laparotomy should remain in bed three weeks has almost disappeared, but there is still discussion as to the exact number of days. I have just read the German view by Kuemmel³ and others, and the French as expressed by Faure⁴ and others. These two surgeons presenting their views before their colleagues take different positions. Kuemmel is an advocate of early getting up, in many of his cases his patients have remained in bed only from one to three days. Faure, on the other hand gives ten days as the minimum.

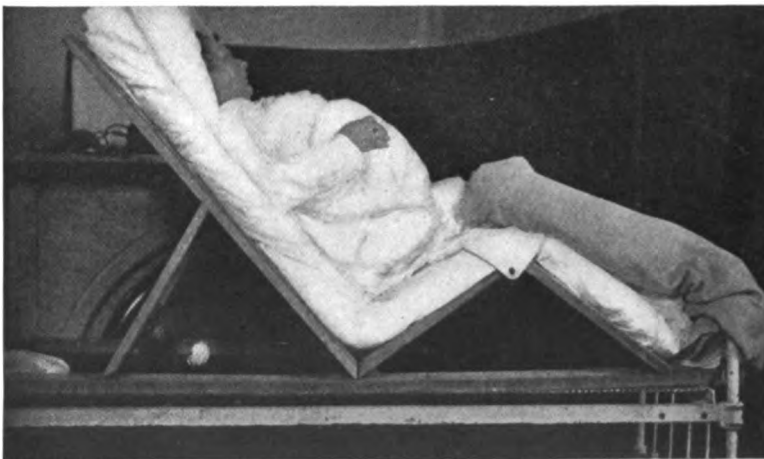
I should advise surgeons to be cautious. In my own experience I found that my patients very ill with peritonitis, who were allowed to move about in bed, were placed in Fowler's position, and had continuous salt per rectum, were more comfortable and

FIG. 1.



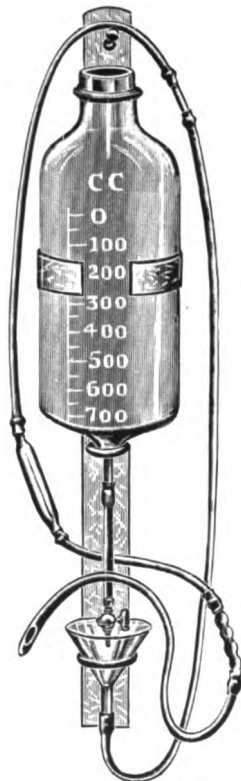
The iron bed in position on the springs of a ward bed. Draw-sheet arranged as for continuous irrigation of bladder.

FIG. 2.



The wooden bed, showing ease with which an extremely heavy patient (250 lbs.) can be kept sitting.

FIG. 3.



Peregrine Wroth's apparatus for proctolysis.

convalesced sooner, in spite of their more serious lesion, than the simple cases of appendicitis in which the patients were kept quiet and for whom it was not thought necessary to give salt per rectum. I was therefore more or less forced to adopt similar procedures with these simpler operative cases.

I can summarize my own experience of the last five years by stating that my patients have been more comfortable, there have been fewer postoperative complications and fatalities and the number of days the patients have remained in bed has at the same time grown less. For this reason, naturally, I must be looked upon as an advocate of the measures in the preparation of patients which I have discussed and the postoperative treatment of sitting position and proctolysis.

POSTOPERATIVE LUNG COMPLICATIONS.—There have been numerous contributions to this subject in the last few years, but nothing especially new. A. Otto⁵ states that he has reduced the percentages very much in the last nine years by adopting careful preparation before anæsthesia and, in addition, he advises the use of a mouth wash, and an inhalation of thymol and alcohol steam twice in the twelve hours before operation. He also employs a special ether apparatus. In addition, he is very careful of all the details of the care of the patient before, during and after operation. Homans⁶ classifies lung complications in three groups, according to the etiological factor: inhalation, hypostatic, and embolic through the lymph-vessels or veins.

It seems to me the consensus of opinion now is that there will be a number of postoperative lung complications over which we seem to have no control. As the actual number of serious and fatal pulmonary lesions is relatively small—I think Otto places the percentage too high at 2.4 to 5.4 per cent.—it is very difficult to estimate the exact value of our preventive measures unless one follows very critically a large series of cases. I am impressed from my own accumulated experience with the fact that it is worth while to exercise great care and judgment over all the minor details of the preparation of the patient before operation, the technic of narcosis and wound treatment during operation, and the postoperative measures which I have discussed. Do not wait for complications to begin treatment, but let your therapeutic measures be of a preventive character from the onset.

Monroe⁷ of Boston, in his address as chairman of Section on Surgery of the American Medical Association, reviews the pulmonary complications of 1000 laparotomies and finds his mortality about 1 per cent.; 11 cases with four deaths, giving a mortality of 0.4 per cent. This can be contrasted with Otto's figures, and Monroe takes the same view as I have taken here when he writes: "Possibly, our routine methods in preparation, etherization and after-care may be a factor of some moment."

PULMONARY EMBOLISM.—Apparently we are no nearer the actual etiological factors of phlebitis with its resultant thrombosis and its possible pulmonary embolism. Bidwell⁸ reports ten cases in his experience and Gibson⁹ discusses fifteen sudden deaths due to pulmonary embolism which have been observed in St. Luke's Hospital in New York since 1899, a period of ten years.

It is a good plan to remember that this fortunately very rare complication may take place after the simplest operation. Gibson does not look with favor upon Trendelenburg's operation, because he is of the opinion that some cases may recover, and if all were subjected to operation the recoveries would be fewer.

It is my opinion that Trendelenburg's operation should be attempted in well-equipped surgical clinics. Krueger¹⁰ makes the last report. His patient lived five and one-half days after operation and died of other complications. At the autopsy the pulmonary artery was patent and the suture had held.

It is worth while here to note that Trendelenburg's first communication appeared in 1907.¹¹ Here he described his animal experiments and one unsuccessful operation on a human being. Later, before the German Surgical Congress¹² he describes the technic in detail, reports a successful case of the removal of an embolus from the pulmonary artery of a calf, and mentions a second human case operated upon by another surgeon in which the patient lived thirty-seven hours and the autopsy demonstrated that death was due to hemorrhage from the internal mammary artery. Sievers,¹³ an assistant in Trendelenburg's clinic, gives his experience in which he operated within twenty minutes after the first symptoms and removed two large clots. The patient lived fifteen hours.

PAROTITIS.—An inflammation of the parotid gland, on one or

both sides, after operation is a rare, but interesting complication. Orthner¹⁴ and Hadda¹⁵ report cases of their own observation and discuss the literature. It has no significance from the standpoint of prognosis. A few months ago, after the removal of a large ovarian cyst in which there were no adhesions and but a small pedicle to ligate, the patient developed double parotitis. It was interesting, because the first case observed, if my memory serves me, was after a similar operation.

ANÆSTHESIA

Dr. Halsted has remarked recently that the days of ether are numbered and that at the present time at least, nitrous oxide with oxygen is the anæsthetic of choice.

It seems to be the growing opinion throughout the surgical world that we should have expert anæsthetists and for a very much larger field nitrous oxide should be employed. In the communication this year I would like to do my part in encouraging surgeons to get their anæsthetists to employ nitrous oxide more and more for longer operations.

There is a very interesting symposium on anæsthesia in *Surgery, Gynæcology and Obstetrics* for May, 1909, and the literature on anæsthesia before me is immense, but I wish to leave the impression that the two methods of anæsthesia to be more carefully considered are the drop-ether on an open cone, and nitrous oxide with oxygen.

INFECTIONS

The surgical treatment of infections is undergoing modifications. There are two problems: first, the treatment of the local infection, and, second, the therapeutic means employed to combat the general systemic poisoning. As far as the local infection is concerned, we must also bear in mind two factors—one much more important than the other. When the infection is distinctly local it may become general at any moment. Every method of treatment should have in view the prevention of a general infection spreading from a distinctly local one. The second problem is so to treat the local infection that the loss of function in the part involved will be least.

It is very interesting to compare the attitude of the surgical mind towards infections with its attitude towards fractures. Lister, in revolutionizing surgical technic, did so with his treatment of fractures. The original treatment was a simple one—nothing was done beyond swabbing the wound communicating with the fractured bone with pure carbolic acid and covering the wound with lint wet in carbolic acid. Simple as this treatment was the results were marvellous. No matter how you might differ in the explanation of how these results were accomplished, there could be no controversy as to the results. Lister attributed them entirely to the antiseptic action of carbolic acid in preventing air infection. To-day's surgeons are of the opinion that non-interference was as much a factor as the antiseptic. Later on, as surgeons grew more and more bold in operative interference, compound fractures, among other surgical diseases, were subjected to the knife until the climax was reached in Volkmann's clinic, where practically every case of compound fracture was operated upon. Then the pendulum swung back until to-day the attitude of the surgeon towards the compound fracture has returned almost to that of Lister's. In a large group of cases nothing but simple cleansing of the external wound is indicated. In a smaller group of cases operation is indicated, and the nature of the operation varies with each individual case. To-day, therefore, we cannot apply a single rule to every case of compound fracture.

I shall not carry this comparison further, but in the beginning the rule of surgeons towards infections, both local and general, was non-interference. The local inflammatory process was subjected to a treatment of rest and heat; for the general condition, rest, modified diet, and water. The patient was left to combat the systemic poisoning with his own natural resources. There was but one treatment for the local infection—incision of the abscess when it was about ready to rupture. As in compound fractures, so also in infections, operative intervention for the local process was introduced earlier and earlier in the inflammatory process, and the incisions and points of drainage were enlarged. There is no doubt that the principle of early and free incision in all local infections is the safest course for the patient with but very few exceptions. There are some infections that are best

let absolutely alone: one is anthrax, and the other is an infected thrombophlebitis.

The modern surgeon, in order to combat local infection and general systemic poisoning, should familiarize himself with the more recent literature on the inflammatory process, on the different local infections, on the research work in immunity, and on the experience with the vaccine treatment, and should more carefully consider the hyperæmic measures of Bier in which are employed the elastic bandage or the suction apparatus.

There is no doubt that we can combat many infections with as good an assurance of a cure and with less local interference than before. That is, we can, in certain selected cases, return somewhat to the attitude of non-interference of the older surgeons. This more modern method, however, requires familiarity with the newer views on inflammation and immunity and with the technic of the newer therapeutic measures.

SILVER SALTS.—The use of silver salts, credited chiefly to Credé, receives less and less attention in recent literature. I have not employed it for a number of years. Proshanski¹⁶ discusses the bactericide action of silver, and Shatski and Gryasnow¹⁷ the intravenous injection of nitrate of silver in the treatment of surgical infections. Proshanski, in his experimental work, demonstrated that the effect of silver solution in water is just as good as when in solution with ascitic or hydrocele fluid. The action of the salts on the *Staphylococcus aureus* is small, but on the typhoid bacillus much more definite. He concludes that the introduction of silver salts up to 0.03 Gm. per kilogramme will be very effective in typhoid fever, almost specific. Shatski and Gryasnow report their experience with 28 cases treated after the method of Hume. Some seven or eight years ago, Hume, then assistant resident surgeon of the Union Protestant Hospital in Baltimore, employed his method in a number of cases, in some of which the recoveries seemed to be due to the intravenous injection of silver nitrate. He employed a 1:10,000 solution and gave intravenously from 200 to 500 c.c. Following his published results there were other reports in the literature, then the method seemed to be given up. One thing can be said in its favor,—that if employed carefully in this way, there is no danger. I should still advise it in cryptogenic general infections.

ANTIFERMENT TREATMENT.—Kolaczek¹⁸ gives a further report on the antiferment treatment of acute abscesses combined with aspiration. After aspirating the abscess there is injected into it an albumin-containing serum such as hydrocele fluid or ascitic fluid. He has even employed it in empyema. From the standpoint of the patient this is a much simpler treatment than free incision and drainage. There is considerable literature from Von Brun's clinic on this subject, first, by Mueller and Peiser,¹⁹ and later by Kolaczek.²⁰ I shall not go into details, but bring this literature forward as emphasizing a line of experimental and practical investigation which has for its object the simplification of the treatment of surgical infections. This treatment does not give a better result than the incision of an abscess, but in some cases just as good a result and with no greater danger from general infection; the patient is saved time and the discomfort of the frequent dressings that drainage demands. In the treatment of empyema it may prove of even greater value. Borszéky and Turàn²¹ report their experience with eighty-five cases. Like Kolaczek and his associates they obtained results with acute abscesses only, and in some of these cases free incision later became necessary. Borszeky and Turan caution against the indiscriminate use of this treatment as it may disseminate the infection if not carefully watched. One must be ready at any moment to introduce incision and drainage.

TRYPSIN-FERMENT TREATMENT IN TUBERCULAR ABSCESSSES.—Borszéky and Turàn have had even better experience with the trypsin-ferment treatment of tuberculous abscesses. This treatment was first advocated by Jochmann,²² and later by Jochmann and Baetzner.²³ The results in tuberculosis of bones and joints have not proceeded far enough to demonstrate the value of the treatment.

VACCINES.—The study of the opsonic index and its vaccine therapy still excites a great deal of interest both in experimental and in practical medicine and surgery. Cole, working in the clinical laboratory of the Johns Hopkins Hospital, came to the conclusion that there were too many factors in the opsonic index to allow its employment with any degree of certainty in the vaccine therapy, but he was also of the opinion that vaccines should be made especially for each case, if possible, and this treatment

tried in certain forms of infection. I cannot go into any detailed discussion of the recent literature, but it demonstrates the point that I am attempting to make, that we are approaching a more scientific treatment of surgical infections. The originator of this method, Wright summarizes his experience and views up to date in the *Practitioner*.²⁴ Coenen²⁵ presents the experience with staphylococcus infections at Kuettner's clinic in Breslau, with the conclusion that the treatment is still in its experimental stage. Hartwell, Streeter and Green²⁶ give their experience with 97 cases treated in the Massachusetts General Hospital in Boston. They were unable to get any results in acute cases; in some of the chronic cases the vaccines seemed to be valuable. They recommend their further trial in puerperal infections. Hollister²⁷ gives a short summary of the cases treated in McArthur's clinic in Chicago. Their results were about the same as in the Massachusetts General Hospital. I would also recommend the reading of communications by His and Zinsser,²⁸ and also by His.²⁹

In the modern treatment of infections the surgeon must be assisted by a bacteriologist. At the present time, for the very acute infections and especially the fatal cases, we have no further armamentarium, but for the more chronic infections, especially those due to the gonococcus and staphylococcus, the vaccine therapy promises results in a certain number of cases which cannot be obtained by any other means.

FEVER.—One always associates fever with infections, and for this reason I call attention here to the very interesting and comprehensive summary by MacCallum³⁰ in a lecture delivered before the Harvey Society. I am of the opinion that every practitioner and surgeon will feel better prepared to treat his cases of local and general infection if he will improve his general conception by reading Adami on Inflammation, MacCallum on Fever, and the other references which I have mentioned in this discussion on the subject of infections, all of which bring out the important points in immunity.

TUMORS

All surgical diseases have their medical aspects. The physician generally sees the patient first. For this reason on him rests the responsibility of selection of those patients who have lesions re-

quiring surgical treatment. The surgeon naturally can keep track of his own results and can estimate the relation between immediate and permanent results and the time after the onset when the surgical disease was subjected to treatment. Therefore, if he finds that he must request the physician to refer to him surgical diseases at an earlier period, it is incumbent upon him also to instruct the physician in the signs and symptoms of the surgical trouble in its earlier stage.

We are beginning to learn in a very practical way more and more about tumors. We are beginning to find out that the number of permanent cures in sarcoma and carcinoma are increasing in proportion to earlier removal. From a surgical standpoint there can be no question of the truth of the statement that benign tumors after years of quiescent growth may become malignant. Therefore, with a certain number of exceptions, a physician should urgently recommend the removal of all apparently innocent tumors which he may find in his routine examinations of patients, whether the patient has consulted him for the tumor or not. The medical aspect of all visible and palpable tumor masses is a simple one: they should be referred to surgeons for treatment. I have again and again written that all tumors should be looked upon as malignant until they are proved to be benign. It is incumbent upon the surgeon, therefore, to prepare himself for the recognition of neoplasms in this earlier state; to know when to enucleate a benign tumor, when to remove it with a small zone of healthy tissue, and when to extend the local operation for malignant tumors. There should be no mutilation unless experience has positively demonstrated that without it there is no hope of a cure. Patients should not be subjected to an extensive operation involving a great risk of immediate death unless positive experience has shown that the possibility of comfort or cure is worth the risk.

The question is often asked of me, whether it is dangerous to excise a piece for diagnosis and then, a few days later, perform the operation. I have just had this question presented to me by Dr. Guerry of Columbus, S. C., who expects to address the Tristate Medical Association on some of the things a physician can do in cases of cancer. There may be, and there undoubtedly are, exceptions to the rule, but my experience has taught me that in some

malignant tumors, practically all carcinomas, it is dangerous to cut into the tumor through healthy tissue, excise a piece, close the wound, and then later perform the indicated operation. If possible the operation should be performed at once. The diagnosis can and should be made from the gross appearance at the exploratory incision, or from a rapid frozen section. I know that some of my colleagues in surgery will take exception to this statement. The only reason for excising a piece for diagnosis is that the surgeon is unable to make one himself and must wait until a competent pathologist does it for him from a well-stained section. It seems to me just that if physicians fulfil the requirements of bringing patients to surgery at a much earlier period in the life of the tumor, they can fairly demand of the surgeon an immediate diagnosis.

BONE TUMORS.—At the last meeting of the American Medical Association in Atlantic City William B. Coley of New York presented before the Surgical Section a paper entitled: "A Plea for More Conservative Treatment for Sarcoma of the Long Bones."⁸¹ In discussing this paper I outlined my own views upon this subject.⁸² I cannot agree with some of the conclusions made by Dr. Coley. I am of the opinion that giant-cell sarcoma is relatively one of the least malignant of the sarcomas of bone and Dr. Coley should not include such tumors in the percentage of cures with his extracts. . . . We have failed to find in the literature a case of pure giant-cell sarcoma which had given metastasis, and there are recorded cures even after two or more operations for recurrence. In the case of medullary giant-cell sarcoma in which I operated in December, 1902,⁸³ the patient has remained free from recurrence up to date—six and one-half years.

The giant-cell sarcoma should not be included in any group of cases in which, in addition to operative measures, other treatment such as Coley's serum or the X-ray has been employed, and cures can be accomplished in this group by the most conservative means without the aid of any sera or the X-ray. The other forms of the less malignant sarcomas of bone are relatively less frequent than the giant-cell sarcoma. . . . when we compare the results in the treatment of the more malignant periosteal and medullary sarcoma with and without the use of the Coley serum we find a great

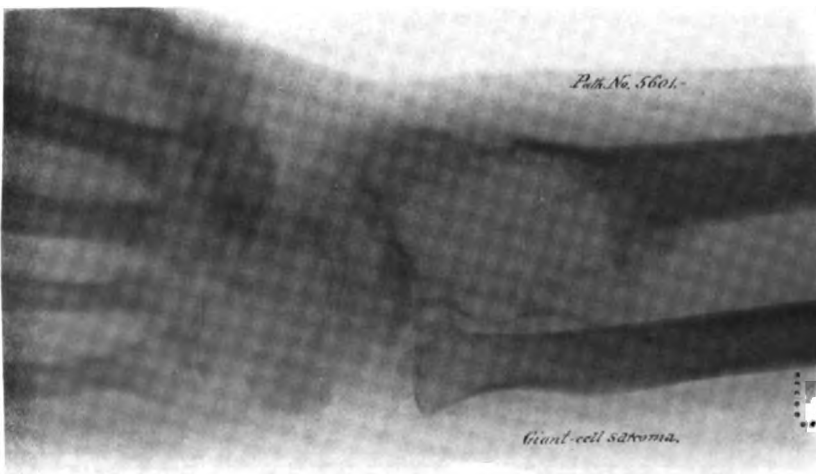
difference. In my experience and in the literature no one has accomplished a number of cures in the round-and-spindle-cell sarcoma equal to Dr. Coley. In view of Dr. Coley's experience I feel that his method of treatment should be tried in all these more malignant sarcomas, so that we may get quickly a large accumulated experience in the hands of numerous investigators. An observation like Dr. Coley's should receive confirmation. In regard to Dr. Coley's statement that a low amputation should be performed rather than a high one, if the serum is employed in addition to operation I would go further. Amputation is only indicated when the complete excision of the tumor would leave a limb without function. It is the extent of the local growth that justifies amputation.

It is a rather remarkable and suggestive observation, which has been commented on by many writers, that among the cures of the more malignant sarcomas of bone there have been about as many resections as amputations. In sarcoma of bone the cause of death is metastasis, not local recurrence. In regard to the question of exploratory incision, I do not see how it can be answered in more than one way. We must explore all early doubtful bone lesions. The surgeon must be his own pathologist, just as will be demonstrated that in surgery of the chest he must be his own physiologist.

Dr. Coley's original article has fortunately arrived in time for me to make a further discussion here. He writes: "I cannot agree with the opinion of Dr. Bloodgood, that myeloid sarcoma is comparatively benign, nor do I believe that it is possible to make a fairly accurate prognosis from the microscopic findings in the various types of sarcoma of the long bones." It is only fair to state that this is not my opinion alone. Practically all surgeons who have studied the pathological aspects of their malignant tumors and all pathologists who have ascertained the clinical picture and the results of the tumors submitted to them for diagnosis now agree in the relative differences in the malignancy both of sarcoma and carcinoma, and that perhaps among sarcoma the giant-cell (myeloid) is the least malignant.

As these giant-cell sarcomas are of such great interest I will reproduce here an X-ray of giant-cell modullary sarcoma of the lower end of the radius (Fig. 4).

FIG. 1.



X-ray of a giant-cell medullary sarcoma of the lower end of the radius; female aged fifty-two, tumor after trauma four years. Note the abrupt expansion of the lower end of the radius. Amputation. Well fourteen years (patient of Dr. Homer E. Safford, of Detroit, Mich.).

20

TENDONS

Jones,³⁴ from an experience of 260 cases of tendon transplantation, concludes that the wound healing is such a simple procedure that many of the patients can be treated in the dispensary clinic. Some of his important conclusions are as follows: In every case over-correction should be maintained until the new tendon has functioned for some time, there should be no angle in the transplanted tendon, and at the same time it should be attached to periosteum. In the same paper he gives his results in 500 cases of arthrodesis for infantile paralysis, with the conclusion that the best results are obtained after ten years of age, before eight years of age there will be only fibrous union, one cannot be certain of the extent of the muscle paralysis until sometimes three years after the onset, and an operation should not be done until it is clearly proved that the paralysis is hopeless.

SURGERY OF THE JAWS

In the *American Practice of Surgery* (vol. vi, p. 813) I have presented my personal experience with lesions of the jaws. The conclusions there bear out what I have previously written in regard to the proper attitude towards tumors arising from bone in general. The more malignant tumors of the jaws are practically hopeless, while the less malignant can be cured by less radical operations. I am quite confident that in this country too extensive operations with the resultant mutilation have been performed for primary tumors of the upper and lower jaws. Especially is this true of antrum tumors.

There is hardly space here to go into detail, but following are some of the facts.

One tumor was a sarcoma arising in the orbital cavity and producing unilateral exophthalmos. This tumor had been previously operated upon. It had all the clinical features of a malignant sarcoma. I felt, however, that if it was curable at all it could be successfully removed without enucleation of the eye or the upper jaw. I found at the operation that the tumor had broken in and filled the antrum cavity. The tumor was removed from the antrum with the curette. Studied microscopically it proved to be a myxo-

sarcoma; the cellular portion was composed of spindle cells, round, and giant cells. The result six years after operation was most satisfactory.

The epulis, the primary sarcoma arising from the alveolar border of the upper or lower jaw, can be removed with assurance of perfect success without any but a limited excision of the alveolar border of the jaw. The epulis shown in Fig. 5 was cured by the use of the Paquelin cautery without extraction of the teeth on each side of the new growth. Microscopically the majority of these tumors are giant-celled sarcomas.

The adamantine epithelioma is histologically as malignant as any other carcinoma. We see, ramifying without any special arrangement in a connective tissue stroma, these peculiar epithelial cells which arise from the enamel organ. Yet these tumors may grow to great size and not infiltrate but remain more or less encapsulated. They do not metastasize. Cures have been accomplished after a number of recurrences, so that one is justified in restricting the extent of the operative removal.

The ossifying periosteal sarcoma of the lower jaw (Fig. 6) and the periosteal fibrosarcoma which may arise from the lower jaw, or in the antrum cavity of the upper jaw, are curable tumors.

In a large experience with carcinoma of the antrum arising primarily in the antrum, or secondary to nasal epithelioma I have never observed a cure, nor have I seen one reported in the literature. The most extensive recent monograph which contains most of the literature up to date is by Perthes.³⁵

The more malignant spindle-and-round-cell sarcoma which occurs as a periosteal tumor of the lower jaw and an antrum tumor of the upper jaw has up to the present time not been cured by the most extensive dissections.

The cystic tumors of the upper and lower jaws which are distinctly benign should be treated by incision and drainage only. These dentigerous cysts which have a thin bony capsule and may give to the palpating finger so-called parchment crepitation, cannot always, in the early stages, be differentiated in clinical history or examination from sarcoma. In tumors of the jaw one should, therefore, before proceeding with a radical operation, make an

FIG. 5.



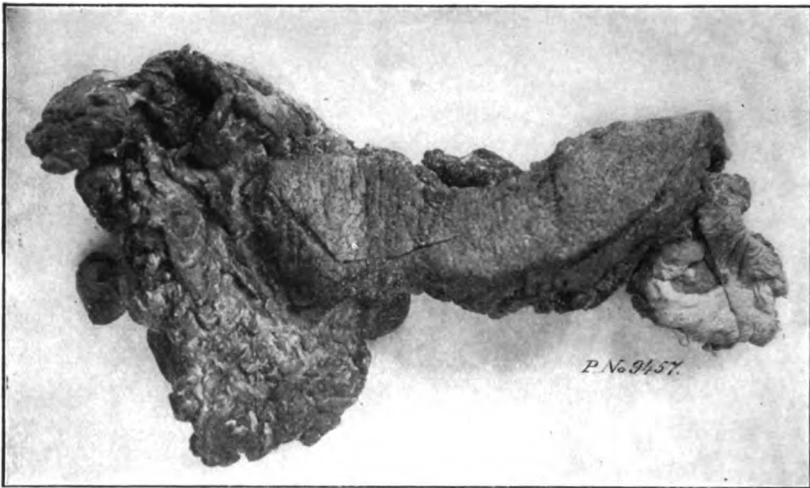
Recurrent epulis (angiofibroma) in a boy of ten.
(American Practice of Surgery.)

FIG. 6.



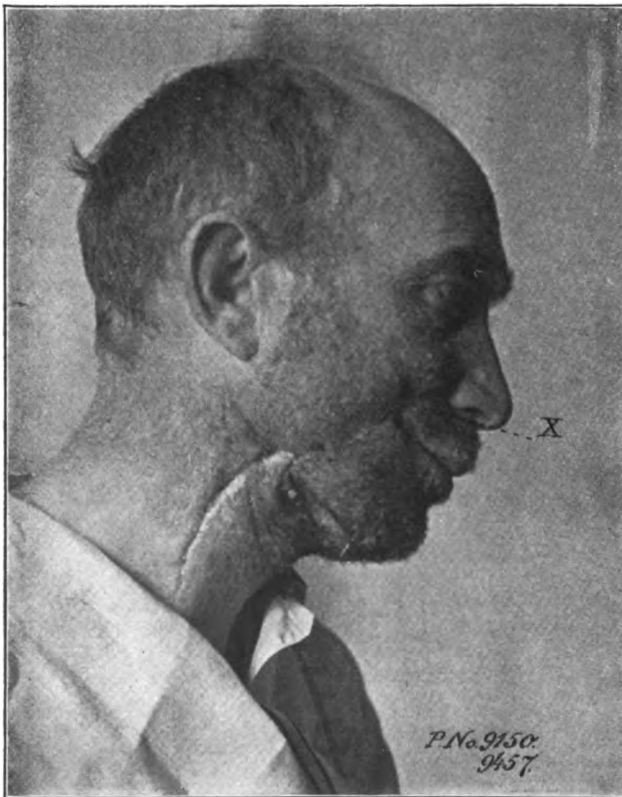
Periosteal osteosarcoma of lower jaw of colored female, aged 13. The tumor has existed 2 months, and the X-ray picture was made after the specimen had been placed in alcohol *(American Practice of Surgery).*

FIG. 7.



Photograph (by Schapiro) of alcohol specimen showing tissues removed in a carcinoma of the gum of the upper jaw (see Fig. 8) (*American Practice of Surgery*).

FIG. 8.



Photograph (by Schapiro) of patient three weeks after operation, at which specimen shown in Fig. 7 was removed; X, position of tumor on gum. (*American Practice of Surgery*.)

exploration and at this the diagnosis. For some of these, *e.g.*, the dentigerous cyst, a very limited excision or simple drainage will accomplish a cure. For others, *e.g.*, the giant-cell sarcoma, the removal with the curette and the Paquelin cautery will promise freedom from recurrence with the least mutilation. For the more malignant, but yet curable sarcomas, and for the adamantine epitheliomas the surgeon need carry his dissection but a few millimetres beyond the capsule of the tumor. For the more malignant sarcomas and for the carcinoma of the upper jaw one may attempt the most radical excision. If these cases are seen early, perhaps the patient will be given a certain number of months of comfort. However, if seen late, one does not add to their comfort by operative treatment. If the surgeon is in doubt as to the differentiation between the curable and incurable sarcomas, it is my opinion that the greatest good can be done to the greatest number with the least mutilation by following conservative lines.

For primary carcinoma of the mucous membrane of the gum of the upper and lower jaws an entirely different attitude is indicated. Experience has demonstrated that cures occur only when there has been an extensive local excision combined with the dissection *en bloc*, of all the tissue surrounding the lymphatic glands which drain the area of the primary growth. Primary carcinoma of the mucous membrane of the gum of the upper and lower jaws is not an infrequent occurrence. I have observed it chiefly in the region of decayed or extracted teeth, I have never seen the tumor arise about perfectly healthy teeth. Fig. 7 represents a dissection *en bloc* of a primary carcinomatous ulcer on the mucous membrane of the gum of the right upper jaw with a zone of cheek, skin and mucous membrane, and the glands of the right side of the neck. In this case the glands were involved. Fig. 8 shows the result in which the mutilation, notwithstanding the extensive resection, is relatively slight. This patient has remained well two years since operation.

SURGERY OF THE STOMACH

ACUTE DILATATION.—Since I went over the subject carefully in 1907,³⁶ the literature has increased so that the rare complication has been given considerable publicity, and surgeons throughout

the world are familiar with the danger of this complication and know that the most important treatment is the early use of the stomach-tube. In very recent American literature there is reported a very interesting recovery after gastrostomy. Very few cases have recovered after a second operative intervention when the dilatation was postoperative, or when the operation was primary for those cases of acute dilatation which are now and then associated with typhoid, pneumonia, rheumatism and other severe illnesses. It is interesting to note that in this case, which recovered after gastrostomy, the surgeon writes that the patient refused to have the stomach-tube employed. It is only natural to infer that he might have recovered without the gastrostomy if the stomach-tube had been used. Now and then, however, it may be impossible to pass the stomach-tube. In one of the six cases reported by MacGonagle,³⁷ a number of attempts with the stomach-tube failed; for that reason the incision which had been made through the right rectus for a cholecystostomy was reopened under local anaesthesia; the balloon stomach presented itself and the gas and liquid contents were evacuated with the trocar, but gastrostomy was not done. The patient recovered. In this instance the symptoms of dilatation were not observed until the tenth day. In the most recent German article by Hans von Haberer³⁸ we find that the etiological factors in acute dilatation of the stomach or gastromesenteric ileus are still awaiting solution. The most important practical point to give publicity to is that this complication may occur at any moment as a postoperative lesion, or as a primary one in general diseases, and that its recognition is not difficult. With the epigastric distention there is always early prostration of the patient, but vomiting may not be present. The stomach-tube should be used at once.

CHRONIC DILATATION.—It is probably incorrect to place gastropnoia with chronic dilatation, but in a few of the recent articles on gastromesenteric ileus previous ptosis of the stomach has been mentioned as an etiological factor. In the cases which I have studied until 1907 I could not convince myself that true ptosis had anything to do with it, although in some cases a chronic gastric dilatation from an old pyloric or duodenal ulcer might have been an etiological factor. In the more recent cases this complication

of acute dilatation after a posterior gastro-enterostomy for chronic dilatation with stenosis of the duodenum or pylorus stand out fairly prominently.

In a recent communication by Sam Weiss⁸⁹ on the operative treatment of gastropotosis I am interested to see a revival of the work of Rovsing first published about ten years ago. Rovsing excludes from his cases of gastropotosis which he subjects to operation those associated with a pendulous abdomen; here the treatment is by an abdominal bandage; those associated with stenosis and dilatation must be relieved by a plastic operation at the pylorus or a posterior gastro-enterostomy. In his narrower group the condition is seen in younger people without pendulous abdomen.

This is undoubtedly a group of cases in which to-day we are very much interested and which I shall discuss again under the subject enteropotosis, but I wish to mention here Weiss's description of Rovsing's operation, a modification of one devised by Duret in 1896.

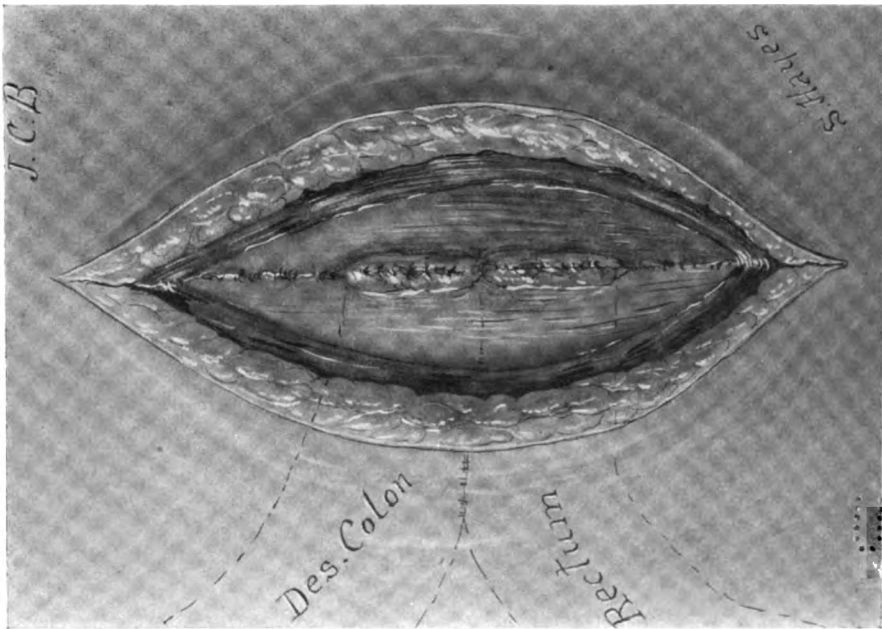
In Weiss's case the symptoms were typical. The patient was thin, neurotic, and suffered discomfort after eating, which was relieved now and then by vomiting. Studied with the X-ray the ptosis of the stomach was easily demonstrated. At the operation the lesser curvature was below the level of the umbilicus and the non-dilated stomach could be easily pushed into the pelvis. Here we have, therefore, an example of an extreme degree of ptosis without dilatation.

Three silk ligatures were passed into the wall of the stomach superficially; each suture caught the stomach three times, so that they covered a distance of about 6 cm. from a point just below the lesser curvature to a point about 3 cm. above the greater curvature. When these sutures were drawn out of the wound the stomach was lifted into its proper place. Instead of passing these stitches through the abdominal wall the peritoneum of the stomach and abdominal wall were sacrificed, and the wound in the middle line closed in the usual way; then the stitches were tied over a glass plate protected with several layers of muslin. The principle of the operation, of course, is to fix the stomach to the anterior abdominal wall at its normal level.

SURGERY OF THE LARGE INTESTINE

TUBERCULOUS TUMORS.—In view of the great improvement in the technic of resection and suture for malignant tumors of the large intestine, this operative treatment has been extended to the tuberculous tumors. In the past the literature has quite frequently called our attention to tuberculosis of the cæcum or at the ileo-cæcal junction. This form of tuberculosis is frequently called hyperplastic, because the inflammatory reaction set up by the tubercular ulcer gives rise to a great thickening of the wall of the cæcum about the ulcer. In one of my cases I found an anastomosis between the ileum and the tip of the appendix, and the dilated appendix carried the fecal contents, because the ileo-cæcal valve was closed. Kuettner⁴⁰ brings together for the first time the tuberculous tumors of the ascending colon which, although less frequent than those of the cæcum, are yet not uncommon. Within eighteen months he observed, and operated upon, four cases in his own clinic in Breslau, and found a fifth among the records of his predecessor, Von Mikulicz. In tuberculosis of the cæcum and ascending colon the clinical picture resembles that of carcinoma. One does not become suspicious of the nature of the disease unless there is tuberculosis of the lungs. When the abdomen is opened it is often impossible to differentiate the hard, nodular tumor from carcinoma, and the diagnosis is frequently not made clear until sections of the mass are examined under the microscope. It is interesting to note that the glands are usually enlarged, but seldom show tuberculosis. Resection is indicated, if the condition of the patient warrants it, because it is difficult to differentiate the tumor from carcinoma. In the clinical history the signs and symptoms differ very little from those observed in carcinoma of the colon. In going over Kuettner's five cases and the eleven cases which he found without difficult in the literature, one is impressed with the fact that complete obstruction is not as frequent a result as in carcinoma. The symptom of onset is usually attacks of colic associated with constipation, until the discomfort becomes so great that the patients restrict their food. Later the palpable tumor appears; in some cases diarrhoea, in practically all cases, if the stools are examined, blood will be found. The results of the operative treat-

FIG. 9.



Sketch of the method of including the closed inverted ends of the descending colon and rectum in the suture of the parietal peritoneum of the wound.

FIG. 10.

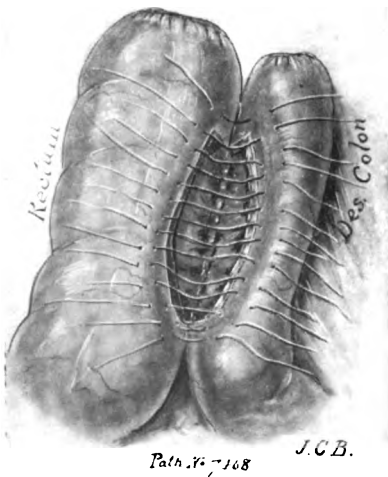


FIG. 11.



Sketch of the method of lateral anastomosis between the smaller descending colon and larger rectum.

ment are excellent if tuberculosis of the lungs is not present. Brunner⁴¹ considers the subject of tuberculosis, actinomycosis, and syphilis of the gastro-intestinal tract a work which is too extensive to review here, but one which should be referred to, because at the present time we have as yet nothing corresponding to it in English.

CARCINOMA.—There are two distinct problems in the lesions of the large intestine: the medical problem which has for its object the building up of a clinical picture which will allow an earlier recognition of this disease, and the problem for the surgeon which has for its aim the mastery of the technical details of the resection and the proper suture. Before the last meeting of American Surgical Association William J. Mayo⁴² presented a review of his one hundred cases. One will find here a discussion of the surgical problems. In this paper Mayo was not at all satisfied with his method of anastomosis after resection. I took the opportunity, in discussing the paper, to direct attention to a method of anastomosis which I published in the *Annals of Surgery*, for February, 1909.

The operating surgeons with experience in intestinal suture and resection are unanimous in the opinion that lateral anastomosis is safer than end-to-end anastomosis. The fault is not with the method of suture, but is due to the impaired circulation in the ends of the resected gut, no matter how carefully the point of resection is selected in relation to the supplying vessels. This is true of both small and large intestine. It occurred to me, therefore, some years ago that the ends of the resected intestine could very easily be sutured just outside the peritoneum in the wound, with a lateral anastomosis beneath. In looking over the literature I find that the method corresponds very closely to the idea of Von Mikulicz, who after resection brought the two ends out of the wound and later accomplished anastomosis by clamping the spur. Both methods have proved successful, and I am informed by Dr. Mayo that he has adopted it in his recent work. The illustrations (Figs. 9, 10 and 11) explain the method. In cases where the obstruction is acute and one wishes to leave an open bowel for drainage a tube can be sutured into the proximal gut.

The medical aspects, however, of tumors of the large intestine,

whether they be of tuberculous, inflammatory, or carcinomatous nature, are very important. We are beginning to learn that carcinoma of the large intestine is among the least malignant forms of carcinoma. The number of permanent cures after gastrectomy is still relatively small, while the number of cures after resection of the large intestine is relatively large, but many cases do not come to surgery until the patients are very ill with acute intestinal obstruction on one hand, or cachectic from extensive infiltration of the tumor on the other. I have recently gone over very carefully the clinical picture of the cases which have come under my observation. In a very few instances the first symptoms have been those of intestinal obstruction. The patients have then come for operation immediately, or have recovered from the obstruction and sought advice later. I am always suspicious of a new growth when I obtain a history of a pretty definite attack of acute intestinal obstruction (obturation ileus) which recovers spontaneously. I find from Kuettner's cases that this has been observed in tuberculosis. In the majority of patients, however, there are prodromal symptoms which, I think, justify an exploration of the abdomen before the appearance of the palpable tumor or before an attack of obstruction. These symptoms are attacks of abdominal pain, usually associated with constipation, now and then with blood in the stools. In all of the cases this history was obtained. If clinicians would bear in mind this possibility when their advice is sought by patients over thirty giving these symptoms, I am confident that a larger number of malignant and tuberculous tumors of the intestine would come for operation at an earlier and more favorable period.

SURGERY OF THE GALL-BLADDER

ANATOMY.—The most interesting contribution since that of Brewer⁴³ is by Ehrhardt,⁴⁴ who describes Luschka's glands. I call attention to this communication, because in my recent experience I was at first confused by a hypertrophy of these glands simulating carcinoma. If I had not been familiar, from recent reading, with Ehrhardt's contribution, I might have persuaded myself to perform an unnecessary cholecystectomy. I am sorry that copyright laws prevent me from reproducing Ehrhardt's illus-

trations. In the normal gall-bladder these glands first described by Luschka, are insignificant, but in chronic hydrops of the gall-bladder the little communicating ducts lined with mucous membrane also dilate, and there may be formation of minute stones; the dilating duct may extend to the peritoneal coat and perforate; the stone which has formed in it may thus get outside the gall-bladder. In the early days of gall-bladder surgery operators marvelled at finding stones, especially in the form of sand, in the adhesions or adherent omentum outside the gall-bladder. The probabilities are that all of these arrive at their extramural position through the diverticulum formed by the dilatation of Luschka's glands.

The secretion of Luschka's ducts resembles the material that one sees in a colloid adenocarcinoma. This summer, in exploring a gall-bladder in which there was a history of recurrent gall-stone attacks, I found an enlarged gall-bladder with a thickened wall. On opening the gall-bladder, I found the viscid white-of-egg secretion that is seen in chronic hydrops. In exploring the cystic duct for stone I brought away, at first to my surprise and discomfort, a quantity of material that made me fear I was dealing with a colloid adenocarcinoma. Even the frozen sections at first sight suggested this, but on more careful inspection I came to the conclusion that at least I would give the patient the benefit of the doubt and drain the gall-bladder. Later when this material was studied after more careful fixation and section, carcinoma could be excluded. This case has suggested to me that possibly in some of the so-called cured cases of carcinoma of the gall-bladder after cholecystectomy in which the malignant adenoma was found only at microscopic study in the wall of the gall-bladder, dilated and branching Luschka's ducts may have been mistaken for carcinoma.

CARCINOMA.—This subject naturally comes up here. Mayo⁴⁵ among 319 cholecystectomies discovered, only after microscopic examination, three cases of carcinoma—about 1 per cent. At the time of the publication these cases had remained well.

Sherrill⁴⁶ in bringing the literature up to date reports four cases. One can feel certain from Sherrill's microscopic illustrations that he is dealing with carcinoma. As the chief

indication to-day for cholecystectomy is the removal of those thick-walled gall-bladders in which the surgeon feels that carcinoma is a possibility, this subject should be given particular attention. Since so many of the problems of gall-bladder surgery have been settled, it is fortunate for the maintenance of our interest in this branch that the subject takes a more prominent position in our minds. Moynihan some years ago found among 18 very thick-walled gall-bladders one carcinoma, and had observed carcinoma twice after cholecystostomy with the conclusion that carcinoma was present at the time of the operation. In the Jubilee number of the *Annals of Surgery* (December, 1909, vol. 1, p. 1265) Moynihan reports a disease of the gall-bladder requiring cholecystectomy. From his colored illustration I am inclined to the view that he is dealing with what Ehrhardt described—dilated Luschka's glands, because in conclusion he states that he finds fine grains of calcareous material imbedded in the mucosa. There is no microscopic study. Ehrhardt in similar cases found that this calcareous material rested in an epithelium-lined duct. Prosser⁴⁷ records a case of carcinoma cured by drainage of the gall-bladder. Here also, it seems to me fair to conclude, that he was dealing with dilated Luschka's ducts. The patient, a male aged twenty-two, was suffering from a chronic hydrops. At the first operation the gall-bladder was drained and a piece of the wall excised for microscopic study. A diagnosis of cancer was made. When the abdomen was explored three months later the gall-bladder had entirely disappeared. Knaggs⁴⁸ is of the opinion that in his case carcinoma followed cholecystostomy. At the first operation the gall-bladder was drained, but on account of a fistula there was a second operation seventeen months later, when carcinoma was found in the gall-bladder. The surgeon here is of the opinion that there was no evidence of carcinoma at the first operation. Payr,⁴⁹ whenever he concludes that there is any possibility of carcinoma, not only performs cholecystectomy, but removes a wide zone of liver including the portal glands. At the present time we have no proof that this theoretically correct conception gives practical results, because apparently so far the very early carcinoma of the gall-bladder has been cured by cholecystectomy, but it is my opinion that the entire subject needs revision after more accurate observations.

PHYSIOLOGY.—A correct knowledge of the flow of bile is of practical importance to surgeons. Howell writes that Bruns⁵⁰ has demonstrated that no bile appears in the duodenum as long as the stomach is empty; when, however, a meal is taken the injection of the chyme into the duodenum is followed by the injection of bile.

When a gall-bladder fistula, after cholecystostomy, with a patent common duct, is slow in healing, theoretically, if the patient was fed every two hours night and day, food would be injected into the duodenum more frequently, the sphincter of the common duct would be more apt to relax, bile would find less resistance to its flow into the duodenum, and there would be less backing up into the gall-bladder. This method, first employed by Jaboulay, is commented upon by Patel⁵¹ and Gross,⁵² who report cases in which they have observed practical results from this method of feeding. I have also had a few cases, and in each instance the constant feeding of the patient, night and day, has been followed almost immediately by a diminution of the flow of bile through the biliary fistula. In one patient it acted almost like magic. I saw this individual six weeks after his cholecystostomy; the operation had been done for a post-typhoid chronic cholecystitis with gall-stones; the common duct had been found free; in addition to copious flow of bile there was marked dermatitis; the patient had been kept on a rather restricted diet with no feeding at night. When fed ever two hours there was a change observed in the flow of bile at once; after twenty-four hours there was very little, and after forty-eight hours the wound had closed and the skin healed.

When the flow of bile comes from the drainage of the liver, this method, of course, will not have any effect, but Gangitano,⁵³ in one of his cases in which there was considerable flow after the drainage of an echinococcus cyst, injected adrenalin into the wound with good results.

HEMORRHAGE INTO THE GALL-BLADDER.—This is very unusual. Pereira-Harris⁵⁴ reports a case. The patient was in collapse, there was a painful gall-bladder tumor; at operation the gall-bladder was distended with blood and stones.

RUPTURE OF GALL-BLADDER.—This also is a rare complication. I have observed it in a post-typhoid acute cholecystitis. This case

is of unusual interest, because it was one of the first to be diagnosed. The patient was first seen by Dr. Osler and referred to Dr. Halsted for operation. On opening the abdomen, the rupture was found to be leaking, and there was general peritonitis which proved fatal. This possibility should be borne in mind in all typhoid patients who exhibit symptoms of cholecystitis. Although many of these cases recover without operation, yet, if one delays too long the gall-bladder may insidiously distend and rupture. Grant⁵⁵ has observed a rupture of the gall-bladder from vomiting; the patient died from peritonitis.

CHRONIC EMPYEMA.—The case reported by Mellish⁵⁶ is of unusual interest and, as far as I know, the only one on record of such long duration. The patient, a woman aged forty-three, had had a gall-stone attack at thirteen years of age, thirty years before, since which time there has always been present a definite palpable tumor. At operation the cystic tumor which at first was considered of nephritic origin was found to be a gall-bladder; the cystic duct was strictured, but the cyst contained two gall-stones.

TYPHOID CHOLECYSTITIS.—Deaver,⁵⁷ in 216 cases demonstrated the presence of typhoid bacilli in seven only. He prefers to delay operation when the attack begins during typhoid fever. Max Schuller⁵⁸ reports a rather interesting case. There was no history of typhoid fever. Clinically the picture was that of a chronic cholecystitis, but the stools of the patient contained the typhoid bacillus, as did also the gall-bladder; there were no stones. The onset of a typhoid cholecystitis may be unusually acute. In one of my recent cases the patient, a young male aged twenty-five, in the third week of a mild typhoid fever, was suddenly awakened with intense pain in the epigastrium associated with slight nausea, but no vomiting; the pain was of a character and in a position that I have seen more frequently with a perforation of the stomach or the duodenum or in pancreatitis, but there was less peritoneal shock, and the rigidity was confined chiefly to the right rectus; the leucocytosis was 15,000 with a definite increase of the polymorphous leucocytes. It seemed to me that a perforation of the small intestine could be excluded, but I feared to delay. Five hours after the onset of the pain—just before operation—I could demonstrate no diminution of the liver dulness, but in spite of this

I felt justified in first making a small suprapubic incision; finding no gas or fluid I felt certain that there was no perforation; then I exposed the gall-bladder through a right rectus incision, found it enlarged, very tense, covered with fibrin, with a dark spot of beginning necrosis at the fundus. It seemed to me that rupture would have taken place at this point in a few hours. The gall-bladder contained dark bile with a great deal of granular débris and typhoid bacilli in pure culture. The patient made a rapid recovery after cholecystostomy.

The observation of Reitter and Exner⁵⁹ is rather unusual. Their patient, in addition to symptoms of gall-stones, had jaundice, and there was a distinct palpable tumor in the head of the pancreas. The typhoid fever dated one year before operation; there had been recurrent attacks; with the last attack great emaciation with enlarged gall-bladder and jaundice. Here we have apparently a post-typhoid pancreatitis. This possibility is also mentioned by Robson and Cammidge in their recent book. Reitter and Exner's patient was relieved by cholecystostomy.

CHOLECYSTITIS WITHOUT STONE.—Riedel,⁶⁰ who has had a very large experience, reports acute cholecystitis with local peritonitis. There are two cases of very acute infection of the gall-bladder of hæmatogenic origin having no relation to gall-stones. In one case the symptoms were so acute (very much as in the post-typhoid cholecystitis just mentioned) that the patient was subjected to drainage of the gall-bladder within twenty-four hours. There was turbid fluid in the peritoneal cavity, and the bile in the gall-bladder was dark and turbid; the patient has remained well eight years since operation. I have observed a similar acute attack after pneumonia, and a second case in which there was a definite relation to a general gonorrhœal infection, but unfortunately cultures were not taken. The post-pneumonic gall-bladder contained the *Staphylococcus pyogenes aureus*. Riedel's second case of infection of the gall-bladder is of interest, because the patient was but nine years of age, and although the abdomen was opened forty hours after the onset, there was evidence of beginning gangrene of the wall of the gall-bladder. For this reason Riedel removed the gall-bladder. The organism proved to be the *Bacillus coli communis*.

One cannot differentiate clinically between cholecystitis with and without gall-stones. This is brought out by Fairchild.⁶¹ Robson is of the opinion that when gall-stones are not present one should prolong the drainage of the gall-bladder on account of the accompanying pancreatitis. I am inclined to think the majority of surgeons will not agree with Fairchild that cholecystectomy is indicated.

INDICATIONS FOR OPERATION.—In the discussion before the International Surgical Congress in Brussels in 1908 Kehr⁶² takes an unusual position. He is of the opinion that by medical treatment gall-stones which are giving trouble can be kept quiescent. Among 4000 cases which he has seen operation was not indicated in 80 per cent. Riedel, Hartmann and Moynihan, representing German, French and English surgical experience, disagree with Kehr, who also takes the unusual position of preferring cholecystectomy when he does operate. In acute jaundice he also delays unless there are chills, fever, and leucocytosis: these indicate cholangitis and immediate operation. In ordinary obstructive jaundice Kehr states that he prefers to delay not more than three months. In this position he stands almost alone.

MORTALITY AFTER OPERATION.—Mayo⁶³ gives the following mortality statistics: "For gall-stones in the gall-bladder (1500 cases), the 'ostomies' (845 cases) had a mortality of about 2 per cent., while the 'ectomies' (319 cases) had 3 per cent. The mortality of common-duct cases is about 13 per cent.; however, in the simple common-duct cases in which there is no infection the mortality is very little larger than in ostomy and less than in ectomy (2.9 per cent). In acute cases with infection, but not complete obstruction the mortality rises to 16 per cent. In the very severe common-duct cases with complete obstruction and marked infection the mortality rises to 34 per cent. It seems to me that figures like these indicate, first, early operations before the stone has reached the common duct, and then, except in special cases, cholecystostomy; and that there should be no delay in jaundiced cases. This is an interesting problem for further study."

GALL-STONES IN CHILDREN.—Friedlaender⁶⁴ reports a case in which the onset of the colic began at four years of age. The child was subjected to operation at six years of age, when stones

were found. Schlesinger and Friedjung (mentioned by Friedlaender) have observed one at four months of age. Rotch, in his recent book on diseases of children states that calculi are so rare that one may mention the possible occurrence only. I have spoken of Riedel's acute cholecystitis without stone in a boy aged nine years. Typhoid fever is not uncommon in children, and perhaps, if children's colics and attacks of transient jaundice were studied more carefully, more cases would be revealed.

GALL-STONES WITHOUT SYMPTOMS.—The frequency with which gall-stones are found accidentally at autopsy have led the profession to the view that there may be no symptoms with a gall-bladder full of stones. Moynihan⁶⁵ is of the opinion that these cases do have symptoms, but the profession needs further education on the early symptoms of gall-stones. If one will study clinically a large number of cases in which the diagnosis is confirmed by operation one will be surprised at the very early symptoms of gall-stones—simply attacks of abdominal pain or indigestion lasting perhaps for years before the typical attacks set in. Murphy⁶⁶ goes over the symptoms in 324 cases.

OBSTRUCTION DUE TO GALL-STONES IN THE INTESTINE WITHOUT HISTORY OF JAUNDICE.—I have removed from the upper jejunum a gall-stone the size of a small hen's egg in a case in which the patient was quite certain that there had never been jaundice and in which there was no history suggesting gall-stone attacks, except attacks of indigestion. The patient was seventy years of age, and the symptoms of obstruction had been present thirty-six hours. The literature contains similar cases. Dickson⁶⁷ reports finding three large gall-stones in the stool of a patient with absolutely no history of jaundice. He is of the opinion that there was a pathological anastomosis between the gall-bladder and intestine.

INTRAHEPATIC CALCULI.—McArthur⁶⁸ is of the opinion that stone may originate in the hepatic duct. In his case we have the picture of cholangitis with jaundice. The patient was not operated on until the twenty-third day of the infection. Clinically it belongs to the most severe type of jaundiced cases, in which Mayo's mortality was 34 per cent. At operation McArthur found pus and stones in the common duct; at autopsy intrahepatic stones in the

hepatic duct. Edwin Beer⁶⁹ in a study of autopsy material found intrahepatic calculi six times. He is of the opinion that there are three factors in the production of these calculi: obstruction, cholangitis, and some unknown factor, and he advises drainage of the duct and gall-bladder in all such cases.

DRAINAGE OF THE HEPATIC DUCT.—Erdmann⁷⁰ in very infected cases (purulent cholangitis) advises irrigation of the duct at operation with salt solution.

RUPTURE OF THE HEPATIC DUCT.—Hildebrandt⁷¹ reports a case in a girl of five in which there was a contusion of the abdomen. The symptoms were rather interesting; the most suggestive was the presence of bile in the urine without jaundice; the patient three weeks after the injury suffered with vomiting, slight abdominal distention with diarrhoea, slight fever and a rapid pulse. The operation revealed that the distention was due to free bile in the peritoneal cavity. There was a definite tear in the hepatic duct which was partly closed by inflammatory exudate. He drained the duct and the patient recovered. Up to this eleven cases have been reported of rupture of the hepatic or common duct, with three recoveries. Wroth, when resident surgeon of the Union Protestant Hospital observed a case which recovered after operation.

OPERATIONS ON THE HEPATIC DUCT.—When the stone cannot be removed it can be crushed, as first suggested by Kocher in 1890 and performed successfully by Mayo-Robson, Delagenière, and recently by Marcel Baillet.⁷² For extensive stricture of the common duct Queny⁷³ united the dilated hepatic duct to the stomach (hepatico-gastrostomy). The patient lived forty-one hours. Kehr⁷⁴ was the first to unite the duct with the intestine (hepato-cholangio-enterostomy)—his patient lived a month. Maylard⁷⁵ also reports a successful case. The anastomosis of the hepatic duct to the stomach or intestine should be tried only when the gall-bladder is in such a condition that it cannot be used for anastomosis.

SURGERY OF THE COMMON DUCT.—Mayo⁷⁶ reports seven cases in which portions of the ducts were lost from various causes. Among these there are three successful sutures to the duodenum. He prefers cholecystenterostomy when it is possible. Moynihan⁷⁷ reports two successful cases of end-to-end anastomosis of the common duct.

TRANSDUODENAL CHOLEDOCHOTOMY.—It is very important to remember that in some cases of stone in the common duct opening the duodenum will allow one to remove the stone, when all other methods have failed. It is not a difficult procedure. The stone can be pushed back into the common duct, the duct can be opened into through the duodenum, or the stone can be crushed. McBurney was the first to recommend it. Berg⁷⁸ reports some interesting experiments upon the cadaver, and in a recent letter (February, 1909) writes that he has performed retroduodenal choledochotomy successfully three times; in each instance there were multiple impacted calculi, and there have been other successful operations by his colleagues in the Mt. Sinai Hospital in New York.

CHOLECYSTOSTOMY.—There is nothing specially new in the technic of this simple procedure. Practically every surgeon of experience has given up suturing the gall-bladder to the abdominal wall. A drainage-tube is sutured in with catgut, protected with gauze. I employ a drainage-tube with a cuff. I have never seen the necessity of turning in the margins as recommended by Mayo and Rockey.⁷⁹ Crouse,⁸⁰ in very adherent and retracted gall-bladders, separates the gall-bladder from the liver and brings over it down to the cystic duct a perforated dental rubber dam. This is a good point to remember.

After the biliary fistula has closed it is important to tell patients that here may be slight recurrent attacks, even with transient jaundice, during the first two months.

CHOLECYSTECTOMY.—Haberer and Clairmont,⁸¹ in their experiments on animals demonstrate that there is a re-formation of the gall-bladder from a dilatation of the cystic duct unless the ligature is tight against the common duct. For this reason they advise, when performing cholecystectomy in man, to place the ligature close to the duct. I would advise the opposite, because in man, if it is necessary to remove the gall-bladder, one should be very glad to see it reformed. I shall not go into the discussion as to the indications of cholecystectomy and cholecystostomy more than to give a few of the recent views. Moynihan and Lilienthal in letters to me of very recent date still prefer 'ectomy' in the majority of cases. Ehrhardt and Moynihan, to whom I have referred when discussing the anatomy of Luschka's glands, speak of

the importance of 'ectomy' because of the possibility of minute stones in the wall of the gall-bladder. This, I think, is very infrequent, and the complication should be recognized when exploring the gall-bladder. In the British Medical Association in 1908, Bland Sutton recommends 'ectomy' in many conditions for which his colleagues would perform 'ostomy.' The majority of surgeons in this country agree with the position of Deaver and Mayo who now prefer 'ostomy,' except in special indications. These indications, it seems to me are best stated by Robson: (1) operable cancer; (2) a useless inflammatory gall-bladder; (3) irreparable stricture of the cystic duct; (4) phlegmonous and gangrenous cholecystitis; (5) empyema—I would add to this, unless there be a stricture of the duct: (6) calcareous degeneration; (7) mucous fistula; (8) gunshot wounds—Ehrhardt would add: (9) dilatation of Luschka's ducts containing calculi (perhaps Robson includes this under calcareous degeneration).

POSTERIOR CHOLECYSTENTEROSTOMY.—I have described Bren-tano's retrocolic method in the review of surgery of the pancreas (p. 287).

ULTIMATE RESULTS AFTER OPERATION FOR GALL-STONES.—Kocher⁸² finds his results unusually good. He has observed but two cases of carcinoma of the gall-bladder and one of the pancreas in which the condition was not recognized at the gall-stone operation. The mortality was low and recurrences rare.

SURGERY OF THE PANCREAS

At the recent meeting of the Southern Surgical Association at Hot Springs, Va., in December 1909, Robert C. Coffey⁸³ presented a very inspiring paper in which he discussed, with illustrations, his attempt to restore the continuity of the pancreatic duct and intestine after resection of the head of the pancreas. He accomplished this by a method of invagination the details of which one must get from the original paper. The object of this experimental surgery on animals is to demonstrate whether resection of the head of the pancreas for carcinoma can be accomplished in a human being technically. In discussing Dr. Coffey's paper I ventured to suggest that instead of attempting an anastomosis of the common duct with the intestine in addition to the anastomosis

of the pancreas with the intestine by his method of invagination, the common duct be ligated and an anastomosis made between the gall-bladder and the jejunum.

This experimental work of Coffey, I trust, will lead to practical results. It is papers of this kind which represent laborious experimental work that stimulate any surgical meeting and add to the interest of the clinical papers. It is of the utmost importance now that experimental investigation and clinical observation go hand in hand.

Le Grand Guerry, of Columbia, S. C., emphasized a point which, in my opinion, is one of the most important questions in surgery of the pancreas to-day, that is, the more frequent performance of cholecystenterostomy. I will discuss this point later. At the same meeting Ransohoff reported two cases of hemorrhagic pancreatitis.

The literature on the pancreas is immense, and before expressing my personal opinion as to the more important features I would like to call attention to the following recent articles. Pilcher⁸⁴ presents a very thorough investigation into the Cammidge reaction. I would recommend the reading of the original. This is a reaction of the urine that must be made by an expert. Cammidge, who writes the chemical part of the last edition of Mayo-Robson on the Pancreas, has great faith in his test. Reports from other sources in England are not so favorable. The latest German report by J. E. Schmidt⁸⁵ is, on the whole, favorable. We need, in practical medicine and surgery, a test for the function of the pancreas, just as we need one for the secretion of other organs, perhaps most urgently for the function of the kidney. Williams and Busch,⁸⁶ in an experimental research again go over the etiology of acute pancreatitis and conclude that there is definite evidence of the fact that regurgitation of the duodenal contents into the diverticulum of Vater associated with gall-stones may produce some forms of pancreatitis.

Licini⁸⁷ has shown a definite change in the thyroid gland after extirpation of the pancreas; the change is along the line of hypertrophy and hypersecretion.

So many cases of pancreatitis which come to the surgeon either in an acute or chronic form give a history of acute epigastric pain

coincident with overindulgence in food and drink and so many of these patients suffer from obesity, that we can draw a fairly definite conclusion as to what hygienic measures should be suggested to such patients with the hope of preventing the graver conditions of the pancreas. We know from physiological investigation that the secretion of the pancreatic juice has a definite relation to eating and to the character of the food. I have been especially struck with this fact, which is also commented upon by others, that the patients who come under observation in very acute attacks of hemorrhagic pancreatitis date the onset of their attack to an unusual overindulgence in food and drink and, in a few cases, without alcohol. These patients do better after operation when starved and given bicarbonate of soda. Physiologically we know that it is chiefly the acid contents of the stomach coming in contact with the mucous membrane of the duodenum that starts the mechanism of pancreatic secretion. Schmidt⁸⁸ observed in a case of pancreatic fistula following the successful excision of a pancreatic cyst a rapid diminution of the secretion from the fistula and a very rapid improvement in the dermatitis when he placed his patient upon a restricted antidiabetic diet and bicarbonate of soda (Wohlgemuth's diet). Goebell and others have also observed this. From my own experience I am convinced that we can influence pancreatic secretion to a certain degree by diet. Patients seen with a history of attacks of epigastric pain not severe enough to justify operation, should be cautioned, and the importance of a careful diet should be explained to them. In cases of pancreatitis to be subjected to operation a preliminary treatment for a few days with antidiabetic diet and bicarbonate of soda should always be insisted upon, and, after operation, this diet should be continued according to the severity of the pathological lesion.

The cause of death in acute hemorrhagic pancreatitis has been demonstrated by laboratory experiment to be due to trypsin alone, or associated with the other ferments of the pancreas. This experimental work may be used as an example of how frequently experimental investigations upon animals is of the utmost importance to practical surgery and medicine. This investigation by Guleke⁸⁹ and Doberauer,⁹⁰ demonstrating the true cause of death can be used as an argument justifying the immediate opening of

the abdomen in all cases in which the clinical picture suggests an acute hemorrhagic pancreatitis. That the patient is in a condition of shock is no argument against immediate laparotomy any more than a shock following the perforation of a gastric or duodenal ulcer should influence one against laparotomy. Many cases of acute hemorrhagic pancreatitis recover completely; others recover from the shock, and the operation is performed from the third to the seventh day for the resultant local necrosis, or later for a hæmatoma, cyst or abscess, but that this group of patients recover cannot be used as an argument against an operation in the earlier stage. When patients with acute hemorrhagic pancreatitis succumb death usually takes place within the first forty-eight hours. I have gone over these cases carefully, I have also examined critically every reported case which has recovered after operation. In the operative technic there are two points on which all the operators agree: removal of the blood-stained peritoneal exudate which always contains pancreatic ferments, and drainage of the pancreas, best accomplished by means of a separation of the omentum and gastrocolic ligament.

From my own experience and from the cases reported in the literature I am quite confident that a diagnosis can and should be made. Within the first twenty-four hours these patients suffer so much pain and show such evidence of depression that the symptoms justify exploration of the abdomen. Many of these cases are looked upon as gall-stone attacks and are given huge doses of morphine, and no doubt in many there is a gall-stone in the diverticulum of Vater. The point that I wish to emphasize is that the symptoms in these cases justify opening the abdomen. Acute hemorrhagic pancreatitis will not always be found. Hawkins observed a rupture of the gall-bladder and a perforated ulcer of the stomach, also an intestinal obstruction, all of which had impressed him as acute hemorrhagic pancreatitis, but immediate operation was indicated in these cases. Other authors have reported acute cases resembling pancreatitis in which the findings have been the same as those of Hawkins.

I emphasize this point, because in two recent articles the patients were not operated upon during shock, but they recovered, and the operation was performed later. The authors conclude

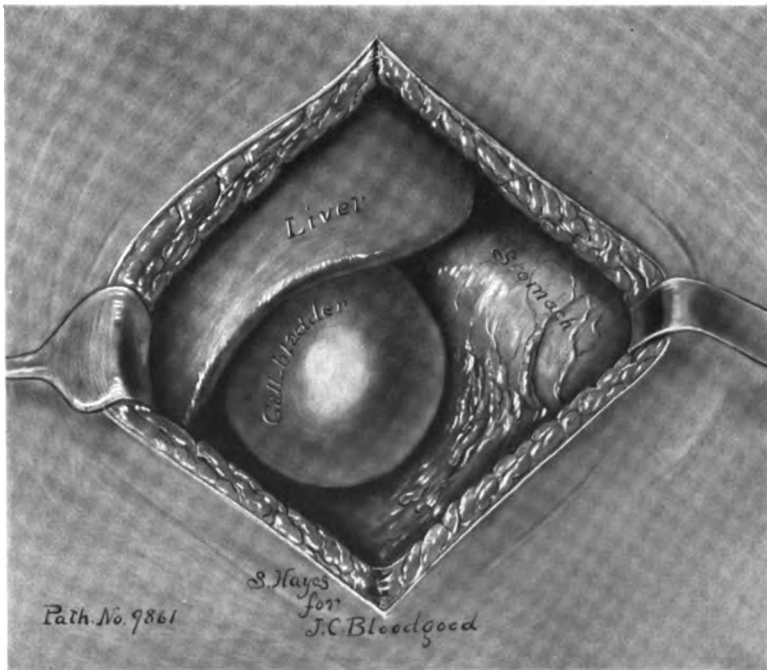
that it was the result of conservative surgery that the patients recovered. I am free to confess that this was my view some years ago, before the experimental work of Guleke and Doberauer.

A suggestion as to the method of operation in these cases which has proved valuable in my own hand is as follows. In doubtful cases make a rapid mid-line incision below the umbilicus. If the case is pancreatitis the fat necrosis will be seen at once on the omentum. In one of my own observations, it was fortunate that I did this, because when I exposed the pancreas in the usual way, it was some time, not until I had reached the pancreas itself through a deep opening made by blunt dissection through a considerable amount of fat in the peripancreatic tissue, before I could demonstrate pancreatitis. It would have required a great deal of courage to make this tedious dissection for drainage except for the fat necrosis revealed by the lower incision only. This lower median incision has other advantages. In critically ill patients it can be done under cocaine or nitrous oxide. If the blood-stained fluid of hemorrhagic pancreatitis is found or if there is an exudate of general peritonitis, we have the best incision for temporary drainage; we can fill the pelvis with gauze wrung out in hot salt solution.

This exploratory suprapubic incision is the best for immediate diagnosis in doubtful cases and the best for immediate and temporary drainage in both pancreatitis and peritonitis. In pancreatitis the wound is closed, while in peritonitis it can be employed for suprapubic permanent drainage if necessary.

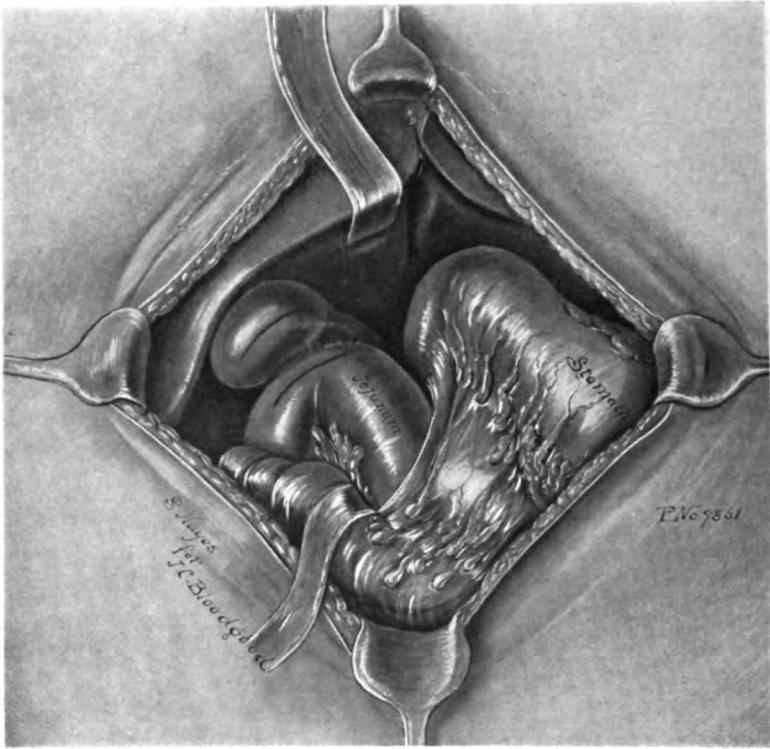
In less acute or chronic lesions of the pancreas I have demonstrated a very rapid and satisfactory way of exploring the pancreas: draw the omentum and transverse colon out through the incision in the right rectus as is done preliminary to posterior gastroenterostomy, and as a rule one can see and feel the pancreas through the thin and semitransparent mesocolon. On two occasions I found fat necroses here and nowhere else. Through this one can outline a pancreatic cyst or abscess and decide upon the best method of drainage. In a recent gunshot wound of the stomach in which I felt quite certain that the pancreas was injured, after suturing the wound in the anterior wall of the stomach, I was at a loss

FIG. 12.



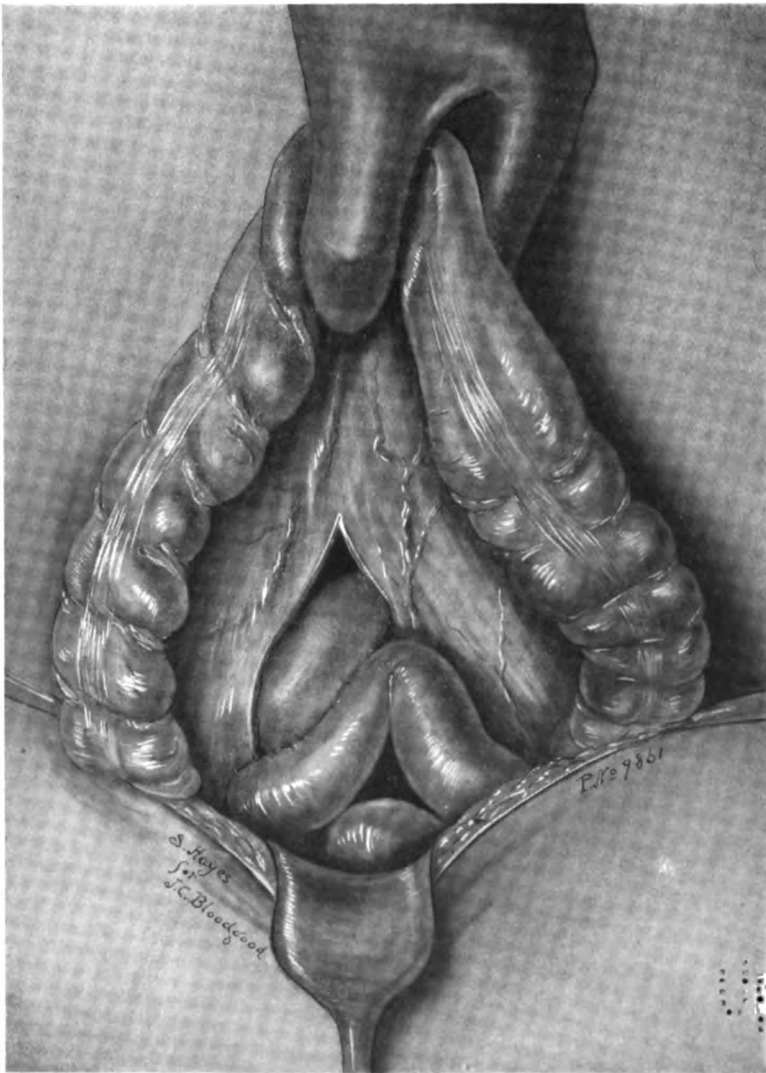
Obstructive jaundice and gall-bladder tumor from chronic interstitial pancreatitis, resembling clinically carcinoma of the pancreas. (This patient was relieved by retrocolic cholecystenterostomy, see Figs. 13 and 14.)

FIG. 13.



The first step of retrocolic cholecystenterostomy. The loop of jejunum is pulled through the slit in the mesocolon preparatory to its lateral anastomosis with the gall-bladder.

FIG. 14.



Cholecystenterostomy—retrocolic cholecystenterostomy. After the lateral anastomosis between jejunum and gall-bladder (see Fig. 13), the jejunum is pulled back and the edges of the slit in the mesocolon are sutured to the gall-bladder. This prevents any obstruction to the jejunum.

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to know how best to get at the posterior wall of the stomach and the pancreas. Experience with posterior gastro-enterostomy induced me to make an exploratory opening in the mesocolon. I found on doing this that I at once exposed the injured pancreas and could cover it with a wet gauze sponge; then I could pull the stomach until I found the perforation near the anterior curvature and closed it. I made a small opening through the omentum and gastrocolic ligament down to the pancreas, and brought gauze through this opening to the pancreas, guiding its proper position by sight through the opening in the mesocolon which was then closed. The patient recovered.

In addition to the question of diet combined with the administration of bicarbonate of soda in pancreatitis, and the influence of the cause of death on the operative treatment of acute hemorrhagic pancreatitis, I am impressed that the next most important problem in this subject to be discussed here is that one brought up by Guerry.

In the first place, the technic of cholecystenterostomy is important. Kehr⁹¹ prefers an anastomosis between the gall-bladder and the stomach, others an anastomosis with the duodenum. Brentano⁹² has applied his knowledge of posterior gastro-enterostomy to devising a method of cholecystenterostomy which impresses me as destined to become the operation of choice. Figs. 12, 13 and 14 are sketches made by Miss Hayes at operation in two of my cases. A slit is made in the transverse mesocolon to the right, in a non-vascular area; the jejunum near the duodenum is drawn through the slit in such a way that its proximal loop, although short, is yet not under tension; the portion of the gut opposite its mesentery is anastomosed with the gall-bladder near the fundus by the ordinary lateral method. If the gall-bladder has been opened for exploration it should be closed unless there is infection, when it will probably be safer to institute drainage through a cholecystostomy. I have performed the operation three times, two patients recovered: one—carcinoma—was absolutely relieved of her symptoms for three months; the other—a case of chronic pancreatitis in which I was unable to dilate the bile duct satisfactorily—is well one year after operation. The third case is a good example

of a not infrequent finding; chronic pancreatitis with jaundice exhibiting all the classical signs and symptoms of carcinoma. This female patient had been jaundiced six months when I saw her; her body was covered with subcutaneous hemorrhagic areas. Four days before operation the usual therapeutic measures to increase the coagulability of the blood were employed. The patient's condition was so critical that I made no attempt at a careful inspection of the pancreas, but rapidly performed the anastomosis. This patient did well three days, bile appeared in the stools; then, suddenly, she showed signs of hemorrhage, blood with stools and from the gums, and blood from the tightly sutured wound. Unfortunately I was unable to get a donor for transfusion. At the autopsy the suture was perfect, the peritoneal cavity was filled with blood clot, the hemorrhage seemed to be due to oozing from the peritoneal surface and the edge of the anastomosis. The pancreas was the seat of chronic pancreatitis, not carcinoma.

It is remarkable how frequently we have the clinical picture of gall-stone with or without jaundice, and find at operation no gall-stones, but an indurated pancreas. Mayo Robson was the first to call attention to cases relieved by simple cholecystostomy, but more recent and extensive experience has demonstrated that this relief may be but temporary. When there is jaundice at the time of the operation and no stones, cholecystenterostomy should be performed; it will be a temporary relief for the carcinoma and a cure for the chronic pancreatitis. When stones are found in the common duct, remember that their removal may not always relieve the obstruction—chronic pancreatitis may be present. It is imperative in every case to pass an instrument from the common bile-duct into the duodenum. If this is found to be impossible or very difficult the anastomosis should be made. In a recent case in which I had no gall-bladder for anastomosis and so many adhesions about the common duct that I felt that an anastomosis with it would be technically very difficult I succeeded in dilating the common duct only after opening the duodenum. When there is no jaundice and no stones I am of the opinion that one should be content first with cholecystostomy; such patients may have recurrent attacks and the more permanent drainage of the biliary system may be forced upon us and then cholecystenterostomy may

have to be done. It is important for surgeons to develop the technic of this anastomosis so that we can demonstrate that it has few elements of danger; at the same time the technic of dilatation of the common duct should be acquired.

SURGERY OF THE SPLEEN

Howell in his text-book on physiology writes, "we are yet in the dark as to the distinctive function or functions of the organ," and again: "the older experimenters demonstrated that this organ may be removed from the body without injury to the animal."

There is, therefore, much of interest in relation to the spleen. Up to the present time surgery has accomplished little beyond splenectomy, and the study of the patients who have survived would lead to the conclusion that no harm has resulted from the removal of the organ. It is a question, however, whether the removal of the spleen in certain blood diseases is of any therapeutic value, except in the fact that it relieves the patient of the discomfort of a tumor and perhaps in Banti's disease the removal of the spleen may check the hemorrhages from the stomach in a mechanical way. George Ben Johnston⁹³ in reporting six cases brings the literature of splenectomy up to date. The more recent article is contributed by Wm. J. Mayo.⁹⁴ He reports ten splenectomies with nine recoveries. One case is of especial interest—a tumor diagnosed lymphosarcoma. The patient was a female aged forty-one and had observed a tumor about four years. In addition to the splenic tumor there was secondary anæmia. Pathologically, it is called a lymphosarcoma. In this case the patient is well three and one-half years after operation. It is fair to conclude from a specific example of this kind that splenectomy of itself has no serious consequences. It is also rather interesting that the tumor is one of the most malignant forms of sarcoma. In my experience I know of but one cure after removal of a tumor which histologically resembled a lymphosarcoma. In this case the tumor had been present ten years before operation, and the patient has remained well eight years since operation. It was situated in the deep flexor muscles of the forearm, it was infiltrating, not circumscribed, and was composed of lymphoid cells in places infiltrating between muscle bundles; in the centre of the tumor there was a hyaline

intercellular substance giving the tumor an alveolar arrangement. Mayo has performed splenectomy twice for Banti's disease with one death. It is rather interesting that in another case in which a clinical diagnosis of splenic anæmia was made, the lesion of the spleen was tuberculosis. In the case of Banti's disease which did not recover from the operation there were a good many adhesions and also a definite cirrhosis of the liver. The patient died of hemorrhage. The recovery after splenectomy for Banti's disease is too recent to judge of the ultimate result. I mention this, because some four years ago I showed before the Clinical Society of Surgery a patient who about two years before had been subjected to an exploratory operation; he had been transferred from the medical ward with the diagnosis of Banti's disease; the spleen was but moderately enlarged; on opening the abdomen I found that the organ was freely movable and splenectomy would have been a very simple operation, but as the patient was not critically ill I felt it was justifiable to try drainage on the principle applied to cirrhosis of the liver. This was done—the patient recovered from the operation—the blood picture changed—and the enlargement of the spleen entirely disappeared. This patient was still well when last heard from—two years ago. If splenectomy had been performed in this case the cure might have been attributed to it.

Van Buren Knott, of Sioux City, Ia., writes me that he has had a successful splenectomy for Banti's disease in a child of five. In his case the convalescence was unusually rapid after operation. Jepson⁸⁵ reports a primary sarcoma of the spleen well one year after splenectomy.*

Dr. Hugh Trout, of Roanoke, Va., has had a successful case of splenectomy for splenomyelogenous leukæmia. In this case the patient was admitted with acute abdominal symptoms suggesting a twist of an ovarian cyst. At the operation the tumor was found to be a huge spleen with its circulation very much impaired on account of a twist. Up to the present time, which is only two months since the operation, there have been no changes indicating any improvement.

It is rather interesting that one of the first successful splenec-

* Dr. Jepson writes me under a recent date that his patient is well.

tomies (Franzolini's case) was associated with the same disease—leukæmia—and this patient is reported cured. According to Johnston (*loc. cit.*) among twenty-eight splenectomies in leukæmia only three patients survived the operation: one lived thirteen days, one eight months, the third is Franzolini's case—so that Trout's is the fourth case.

Robert C. Bryan,⁹⁶ of Richmond, Va., who collects 35 cases and sums up the literature, has observed a spontaneous rupture of the spleen in the third week of typhoid fever; he was unable to find a reference in the literature to a similar case. I find no special literature on this subject. Rupture of the spleen, however, from a contusion, especially of the enlarged spleen in malaria is not uncommon. Lotsch⁹⁷ and Hoffmann⁹⁸ discuss this subject.

It is to be hoped that in this border-line subject—diseases of the spleen—physician and surgeon will work together. It may be possible to do something for this class of cases in the earlier period by an earlier splenectomy or some more conservative measure. It is conceivable that splenectomy very early in a condition like leukæmia might have some specific effect, perhaps enough to check the disease.

It is interesting to note that the spleen has been successfully removed during pregnancy. Schauta⁹⁹ performed the operation during the fourth month for a hypertrophied spleen, and the patient was well three months after operation. Blood counts before operation, after operation, and three months later showed no special changes.

The observation of Kammerer¹⁰⁰ has two points of interest: the intermittent fever with splenic anæmia before operation, and the attacks of convulsions simulating epilepsy on the tenth and thirteenth days in a patient who had never had such attacks before. Three months after operation the patient had gained thirty pounds in weight and the marked anæmia had been replaced by a normal blood count. The evidence in this case is very suggestive that splenectomy was helpful. Morris J. Lewis¹⁰¹ makes a report of interest on account of the careful blood examinations. The splenectomy was done by Dr. Harte in 1904. One will find here a careful study of the blood picture.

In connection with tuberculosis of the spleen there is a case

reported from the University clinic of Palermo by Giaccio,¹⁰² and the subject is brought up to date by Hans Strehl,¹⁰³ who also gives an illustration of the specimen showing large and small caseous tubercles.

Von Herczel¹⁰⁴ brings out an important point in the technic of the operation. If in clamping and ligating the splenic vessels one does not keep closely to the spleen, it is possible, in view of the relation of these vessels to the pancreas, to crush pancreatic tissue, and then the pancreatic juice will cause fat necrosis about the ligatures and may lead to a small abscess. Von Herczel is of the opinion that some of the cases of fever after splenectomy are due to this, and advocates great care in placing the ligatures close to the spleen.

In connection with Trout's case in which the diagnosis was not made until the abdomen was opened, I should refer to Kadygroboff,¹⁰⁵ who in reporting one pedicle torsion of a wandering spleen states that twenty-three cases have been reported in the literature. On account of the acute symptoms not a single case has been correctly diagnosed. A routine blood examination in all cases in which the splenic enlargement is associated with a definite blood disease would allow the surgeon to know before operation that he is dealing with a grave lesion.

SURGERY OF THE ŒSOPHAGUS

In a recent observation the X-ray picture suggested that the obstruction was due to a diverticulum, but the clinical history and the picture that one could get most beautifully with the œsophagoscope looked like carcinoma. I then searched the literature carefully for X-ray pictures of diverticula and stricture to see whether there is any difference. Kuester¹⁰⁶ shows sketches illustrating that there is practically no difference in the X-ray shadow between a diverticulum and the dilatation of the œsophagus above a stricture except that when there is stricture there may be a little tongue-like shadow below the smooth oval shadow of the dilated œsophagus filled with the bismuth emulsion. One of them is the X-ray which compared with others in the literature cannot be differentiated from a diverticulum—this is my case. In a second X-ray of the same case the little tongue-shaped process is

shown. When these X-rays are compared with Kuester's sketches one can see that in his case also the first X-ray shadow resembled a diverticulum, the second, as in my second picture, has the characteristic differentiating shadow. As far as I am able to judge from evidence in the literature this may be looked upon, until we find an exception to the rule, as a differentiated point, at least one to be considered.

Kuester operated in his case without interpreting the shadow and found a stricture. In my case no operation has been done, so as yet the diagnosis is not confirmed. I give below a short résumé of Kuester's communication and also of one by Goldmann.¹⁰⁷

The case reported by Kuester is of interest in its clinical features. The patient was a female aged fifty-seven admitted to the clinic in August, 1906, with a four-year history. After an attack of influenza with bronchitis she noticed that at irregular intervals there was regurgitation of solid food, sometimes with a gurgling sound. She has been growing worse. When she eats rapidly she vomits; when slowly and masticating well she does not vomit. The regurgitated food is undigested and sweet. She has a sensation of fulness in the neck. At night when she lies down and turns on her left side, she regurgitates a certain quantity of food and then feels more comfortable. She also notes that during vomiting there is dyspnœa. There is an irritable cough in the morning, with expectoration. She has also observed a swelling on the left side of the neck. The probe finds an obstruction 22 to 24 cm. from the teeth and to the left, but when passed to the right it can be continued into the stomach. The X-ray shows a pear-shaped shadow in the left side of the neck extending into the thorax. At the operation a ball-shaped sound was passed into the diverticulum and a tube into the stomach. There was no difficulty in exposing the sack; the superior thyroid artery was ligated. Part of the sack was excised, the remainder closed, invaginated and then the slit in the invagination again sutured with catgut. The method of invagination is the same as employed by Kuester for hernia since 1877. This, as applied to diverticula of the œsophagus, was first recommended by Nicoladoni and first employed by Girard. The operation was performed about August 22, and the wound did not completely heal until Sep-

tember 19, but the feeding by œsophageal tube was continued until October 1. The recovery was complete. The patient, however, returned October 18 with a fistula which led into the œsophagus and healed rapidly after injection of iodine and tube feeding. She died the following January apparently of influenza without any further recurrence of the fistula.

Kuester is of the opinion that influenza was the etiological factor in that it paralyzed some of the muscles of the œsophagus and allowed the mucous membrane to bulge out with the formation of a diverticulum. The microscopic picture shows this destruction of the muscular wall. In view of the fistula formation in this case Kuester decided in his next case to invaginate the entire diverticulum.

Kuester's second case presents the clinical picture of a malignant stricture. A male of forty-five gives a history of three months' difficulty of deglutition until he was barely able to swallow liquids. At first he had a sensation of food sticking in his throat, then there was definite local pain and tenderness in the neck followed by retching, vomiting and relief; at intervals he could swallow with less trouble. The obstruction was 24 cm. from the teeth. The first X-ray showed a pear-shaped sack to the left; the second X-ray a sack of 2.5 by 5 cm. extending below the base of the first rib, with broad base below and attenuated upwards. At the operation no diverticulum was found, although the shadow was like the one in the first case in which a diverticulum was found. On opening the œsophagus it was found dilated; lower down the finger met with an obstruction, but a catheter could be passed. This was left in place for feeding, and everything sutured tight around it. The tube was removed on the seventh day; from then until the fourteenth day numerous attempts were made at dilatation from the mouth, with but indifferent success. After an apparently successful attempt with the introduction of a tube the patient developed a cough, chill and fever, and died of œdema of the lung. The autopsy demonstrated a stricture of the œsophagus with dilatation above. The stricture was about 4 cm. long, adherent to the trachea, and a false passage had been made.

Goldmann (*loc. cit.*) in his first case employed the two-stage operation: first gastrostomy and then an attack on the diverticulum.

In his second case in which the diverticulum was situated only at the level of the cricoid cartilage he attacked it directly. In this case the clinical history was rather characteristic of an œsophageal diverticulum. A male, aged fifty-one, had had symptoms since youth: difficulty in swallowing and coughing up, now and then, of meat and other solid food. Twelve years ago he observed a gurgling sound. The diverticulum could be made out with the œsophagoscope. The sack was exposed by an incision, a tube having been placed in the œsophagus. The sack was about the size of a goose egg, and its pedicle was attached to the posterior wall of the œsophagus. The pedicle was ligated with silk, the sack opened, stitched to the skin and isolated with gauze. The sack sloughed, and a small fistula formed which healed in two months. The second part of his paper is devoted to a discussion of the presence of a mouth of the œsophagus at its junction with the pharynx—a condition first discovered by Killian of the same clinic, and one which Goldmann was able to demonstrate when exposing the œsophagus in a thyroid operation, when a ring constriction could be seen at the junction of the œsophagus and pharynx. When the patient was asked to swallow Goldmann could see this ring constriction disappear and the two tubes filled with air coalesce, then the ring reappeared. He is of the opinion that the pulsion diverticula which are always found at this point are really a dilatation of the hypopharynx and rest upon a spasmodic condition of the sphincter of the œsophageal mouth. If food is prevented from entering here it is pressed against the wall of the pharynx, and this has the least support on its posterior wall. Pollard¹⁰⁸ has demonstrated a spasm of this mouth of the œsophagus below the opening of the pulsion diverticulum.

Goldmann is of the opinion that, on account of this spasm of the sphincter at the mouth of the œsophagus there is greater tension on the sutures closing the mouth of the diverticulum. For this reason he still advocates operation in two stages. It may be demonstrated that division or forcible dilatation of this sphincter, the seat of the spasms, may cure the pulsion diverticulum in its early stages.

We have, therefore, examples of a distinct spasm of the sphincter at each end of the œsophagus: the cardiospasm at the lower end

with the resultant dilatation of the œsophagus above it is well known. I should like to call this spasmodic condition of the other end pharyngospasm, and apparently it is the etiological factor in the pulsion diverticulum.

I have called particular attention to these communications and have reproduced my X-rays to illustrate that we need further experience in the study of X-ray shadows of œsophageal lesions.

Max Tiegel¹⁰⁹ presents a most interesting experimental study of the best method of suture of the œsophagus to the stomach after resection for carcinoma of the cardiac end of the stomach or lower end of the œsophagus. The same problem was presented before the last meeting of the American Surgical Association, for which see *Transactions*, xxx, 1909, vol. xxxvii, p. 199; and *Annals of Surgery*, 1909, vol. 1, p. 175.

REFERENCES

1. COLE: *Southern Med. Jour.*, June, 1909.
2. WROTH: *Surg., Gyn. and Obstet.*, Nov., 1909, vol. ix, p. 588.
3. KUEMMEL: *Centralbl. f. Chir.*, 1909, vol. xxxvi, p. 498.
4. FAURE: *Centralbl. f. Chir.*, 1909, vol. xxxvi, p. 711.
5. OTTO: *Centralbl. f. Chir.*, 1909, vol. xxxvi, p. 977.
6. HOMANS: *Johns Hopkins Hosp. Bull.*, April, 1909.
7. MONROE: *Jour. Am. Med. Ass.*, Aug. 7, 1909, vol. liii, p. 425.
8. BIDWELL: *Practitioner*, February, 1909.
9. GIBSON: *N. Y. Med. Rec.*, January 9, 1909.
10. KRUEGER: *Centralbl. f. Chir.*, 1909, xxxvi, p. 757.
11. TRENDLENBURG: *Centralbl. f. Chir.*, 1907, xxxiv, p. 1302.
12. TRENDLENBURG: *Centralbl. f. Chir.*, 1908, vol. xxxv, p. 4 in Supplement No. 35; and *Arch. f. klin. Chir.*, 1908, vol. lxxxvi, p. 686.
13. SIEVERS: *Deutsche Zeitschr. f. Chir.*, 1908, vol. cxiii, p. 282.
14. ORTHNER: *Surg., Gyn. and Obst.*, 1909, vol. viii, p. 850.
15. HADDA: *Centralbl. f. Chir.*, 1909, xxxvi, p. 728.
16. PROSHANSKI: *Centralbl. f. Chir.*, 1909, vol. xxxvi, p. 144.
17. SHATSKI and GRYASNOW: *Ibid.*, p. 164.
18. KOLACZEK: *Centralbl. f. Chir.*, 1909, vol. xxxvi, Supl., No. 31, p. 5.
19. MUELLER and PEISER: *Beitr. z. klin. Chir.*, 1908, vol. lx, p. 236.
20. KOLACZEK: *Ibid.*, vol. lxi, p. 89.
21. BORSZEKY and TURAN: *Beitr. z. klin. Chir.*, 1909, vol. lxiv, p. 387.
22. JOCHMANN: *Virchow's Arch.*, vol. 194.
23. JOCHMANN and BAETZNER: *Münch. med. Wchnschr.*, 1908, No. 48.
24. WRIGHT: *Practitioner*, 1908, vi, 565; reviewed in *Am. Jour. Med. Sci.*, 1909, cxxxvii, 138.
25. COENEN: *Beitr. z. klin. Chir.*, 1909, lxiii, p. 347.
26. HARTWELL, STREETER and GREEN: *Surg., Gyn. and Obstet.*, 1909, vol. ix, p. 271.
27. HOLLINSTER: *Surg., Gyn. and Obstet.*, 1908, vii, p. 629.
28. HIS and ZINSSER: *Jour. of Med. Research*, 1908, xix, 323.
29. HIS: *Arch. Internat. Med.*, 1909, iv, p. 32.
30. MACCALLUM: *Arch. Internat. Med.*, 1909, vol. ii, p. 569.
31. COLEY: *Jour. Am. Med. Ass.*, 1910, liv, 333.
32. BLOODGOOD: *Ibid.*, p. 341.
33. BLOODGOOD: *Johns Hopkins Hospital Bull.*, May, 1903, vol. xiv, p. 133.

34. JONES: *Brit. Med. Jour.*, March 28, 1908.
35. PERTHES: *Deutsche Chirurgie*, Lief. 33a, 1907.
36. BLOODGOOD: *Ann. of Surg.*, 1907, vol. xlv, 136.
37. MACGONAGLE: *Surg., Gynec. and Obst.*, 1909, vol. viii, p. 459.
38. VON HABERER: *Arch. f. klin. Chir.*, 1909, vol. lxxxix, p. 634.
39. WEISS: *Deutsche Zeitschr. f. Chir.*, 1909, vol. cii, p. 537.
40. KUETTNER: *Deutsche Zeitschr. f. Chir.*, 1909, vol. c, p. 212.
41. BRUNNER: Tuberculose Aktinomykose, Syphilis des Magen-Darmkanals, *Deutsche Chir.*, Lief. 46a, 1907.
42. MAYO: *Trans. Am. Surg. Ass.*, vol. xxvii, 1909, p. 311; and *Ann. of Surg.*, July, 1909, vol. l, p. 200.
43. BREWER: *Med. News*, 1903, vol. lxxxii, p. 821.
44. EHRHARDT: *Arch. f. klin. Chir.*, 1907, vol. lxxxiii, p. 1118.
45. MAYO: *Ann. of Surg.*, 1906, vol. xlv, p. 209.
46. SHERHILL: *Ann. of Surg.*, vol. xlv, p. 866.
47. PROSCHER: *Jour. Am. Med. Ass.*, 1907, xlviii, p. 481.
48. KNAAGS: *Lancet*, 1904, i, p. 1054.
49. PAYR: *Centralbl. f. Chir.*, 1908, p. 1341.
50. BRUNS: *Arch. de Sci. Biol.*, 1899, vol. vii, p. 87.
51. PATEL: *Centralbl. f. Chir.*, 1906, vol. xxxiii, p. 195.
52. GROSS: *Ibid.*, p. 197.
53. GANGITANO: *Riforma med.*, February 2, 1907.
54. PEREIRA-HARRIS: *Lancet*, 1906, i, 513.
55. GRANT: *Jour. Am. Med. Ass.*, 1903, xl, p. 1057.
56. MELLISH: *Ann. of Surg.*, 1904, vol. xxxix, p. 570.
57. DRAVER: *Jour. Am. Med. Ass.*, 1906, vol. xlvii, p. 402.
58. SCHULLER: *Wien. klin. Wochenschr.*, 1908, No. 2.
59. REITTER and EXNER: *Centralbl. f. Chir.*, 1908, vol. xxxv, p. 844.
60. RIEDEL: *Mitt. a. d. Grenzgeb. etc.*, 1908, vol. xix, p. 1.
61. FAIRCHILD: *Jour. Am. Med. Ass.*, 1905, xiv, p. 454.
62. KEHR: *Centralbl. f. Chir.*, 1908, xxxv, p. 1339.
63. MAYO: *Ann. of Surg.*, 1906, vol. xlv, p. 109.
64. FRIEDLAENDER: *Centralbl. f. Grenzgeb. etc.*, 1909, p. 42.
65. MOYNIHAN: *Brit. Med. Jour.*, 1907, ii, p. 1381.
66. MURPHY: *Med. News*, 1903, lxxxii, p. 825.
67. DICKSON: *Lancet*, 1906, ii, p. 221.
68. McARTHUR: *Jour. Am. Med. Ass.*, 1905, vol. xlv, p. 1797.
69. BEER: *Arch. f. klin. Chir.*, 1904, vol. lxxiv, 114.
70. ERDMANN: *Med. Rec.*, 1906, vol. lxx, p. 441.
71. HILDEBRANDT: *Arch. f. klin. Chir.*, 1906, vol. lxxxi, p. 647.
72. BAILLET: *Bull. et Mem. de la Soc. de Chir.*, xxix, p. 1194.
73. QUENY: *Bull. et Mem. de la Soc. de Chir.*, 1905, p. 218.
74. KEHR: *Centralbl. f. Chir.*, 1904, p. 185.
75. MAYLARD: *Ann. of Surg.*, 1905, vol. xli, p. 56.
76. MAYO: *Ann. of Surg.*, 1905, vol. xlii, p. 90.
77. MOYNIHAN: *Brit. Med. Jour.*, 1905, ii, 1390.
78. BERG: *Ann. of Surg.*, 1903, vol. xxxviii, p. 275.
79. MAYO and ROCKEY: *Med. Rec.*, 1906, lxxviii, p. 901.
80. CROUSE: *N. Y. Med. Jour.*, 1906, lxxxiv, p. 579.
81. HABERER and CLAIRMONT: *Arch. f. klin. Chir.*, 1904, lxxiii, p. 679.
82. KOCHER: *Arch. f. klin. Chir.*, 1906, vol. lxxxi, p. 655.
83. COFFEY: *Ann. of Surg.*, 1909, vol. l, p. 1238.
84. PILCHER: *Ann. of Surg.*, 1910, vol. li, p. 89.
85. SCHMIDT: *Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, 1909, vol. xx, p. 426.
86. WILLIAMS and BUSCH: *Jour. Med. Research*, 1907, vol. xvii, p. 35.
87. LICINI: *Deutsche Zeitschr. f. Chir.*, 1909, vol. ci, p. 522.
88. SCHMIDT: *Centralbl. f. Chir.*, 1908, xxxv, p. 455.
89. GULKE: *Arch. f. klin. Chir.*, 1906, vol. lxxviii p. 843; and 1908, vol. lxxxv, p. 615.
90. DOBERAUER: *Beitr. z. klin. Chir.*, 1906, vol. xlviii, p. 456.
91. KEHR: *Mitt. a. d. Grenzgeb. etc.*, 1909, vol. xx, p. 60.
92. BRENTANO: *Centralbl. f. Chir.*, 1907, vol. xxxiv, p. 681.

93. JOHNSTON: *Ann. of Surg.*, July, 1908, vol. xlviii, p. 50.
94. MAYO: *Jour. Am. Med. Ass.*, 1910, vol. liv, p. 14.
95. JEPSON: *Ann. of Surg.*, 1904, vol. xl, p. 80.
96. BRYAN: *Ann. of Surg.*, 1909, vol. l, p. 856.
97. LOTSCH: *Deutsche Zeitschr. f. Chir.*, 1908, vol. xciii, p. 90.
98. HOFFMANN: *Beitr. z. klin. Chir.*, 1909, vol. lxiii, p. 786.
99. SCHAUTA: *Centralbl. f. Gynec.*, 1906, No. 25.
100. KAMMERER: *Ann. of Surg.*, 1909, vol. l, p. 484.
101. LEWIS: *Am. Jour. Med. Sci.*, 1908, vol. cxxxvi, p. 157.
102. GLACCIO: *Deutsche Zeitschr. f. Chir.*, 1909, vol. xcvi, p. 464.
103. STREHL: *Arch. f. klin. Chir.*, 1909, lxxxviii, p. 834.
104. VON HERCZEL: *Wien. klin. Wochenschr.*, 1907, No. 5.
105. KADYGROBOFF: *Centralbl. f. Chir.*, 1908, vol. xxxv, p. 454.
106. KUESTER: *Arch. f. klin. Chir.*, 1907, vol. lxxxiii, p. 613.
107. GOLDMANN: *Beitr. z. klin. Chir.*, 1909, vol. lxi, p. 741.
108. POLLARD: *Brit. Med. Jour.*, 1907, vol. i, p. 1039.
109. TIEGEL: *Beitr. z. klin. Chir.*, 1909, lxxv, p. 314.

INDEX TO VOLUME I

(TWENTIETH SERIES)

A

American Medical Association's post-graduate course, 188
Anæsthesia, 257
Anæmia, 216, 248
Anatomy, 171
 of the gall-bladder, 272
Angina pectoris, 222
Antiferments in infections, 260
Antihuman hæmolytic system, 22
Asthma, 212

B

Beck, E. G., The diagnostic value and therapeutic effects of bismuth paste in chronic suppuration, 102
Biliary colic, 212
Bismuth paste in suppuration, 102
Blackburn, J. H., The course of post-graduate study of the American Medical Association, 188
Blood diseases, 216, 248
Bloodgood, J. C., Progress of medicine during 1909—surgery, 252
Bone tumors, 268
Bordet-Gengou phenomenon, 1
Brav, A., Eye-strain among school children, 149
Bronchitis, 214

C

Cambridge reaction, 244
Cancer of the gall-bladder, 275
 of the intestine, 271
Cerebrospinal meningitis, 199, 236
Cholecystectomy, 281
Cholecystenterotomy, 282
Cholecystitis, 276
 without stone, 277
Cholecystotomy, 281
Choledochotomy, 281
Chorea, 225
Circulatory diseases, 218, 249
Colitis, 95
Common duct, surgery of, 280

Conception and vaginal portion of uterus, 171
Constitutional diseases, 202, 240
Cretinism, 205

D

Diabetes, 202, 241
Diagnosis and treatment, 42, 58, 62
 with bismuth paste, 102
 with tuberculin, 62, 66
Diarrhœa, 211
Digestive diseases, 206, 243, 267
Dilatation, cardiac, 221
 of the stomach, 267, 268
Diphtheria, 196, 284
Disseminated sclerosis, 227
Drainage of the hepatic duct, 280
Dysentery, 211, 240

E

Empyema of the gall-bladder, 276
Endocarditis, septic, 220
Epilepsy, 224
Erysipelas, 197
Exophthalmic goitre, 203
Eye-strain in school children, 149

F

Fever and infections, 261
Fulton, Dudley, Chronic mucous colitis, 95

G

Gall-bladder, surgery of, 272
Gall-stones and obstruction without jaundice, 279
 in children, 278
 intrahepatic, 279
 without symptoms, 279
Gastric cancer, 210
 ulcer, 208
Gatch bed, 254
Graves's disease, 203
Gout, 76
Gynæcology, 126, 145

H

- Hæmophilia, 218
 Hæmoptysis, 214
 Halstead, A. E., Tuberculosis of the thyroid gland, with report of a case, 120
 Heart disease, 218
 Hemorrhage into the gall-bladder, 275
 Hepatic duct, surgery of, 280
 Hygiene of menstruation, 148
 Hyperchlorhydria, 207

I

- Indigestion, 206
 Infantile anæmia, 216
 Infections, 257
 surgical, 257
 Infectious diseases, 198, 228
 Influenza, 238
 Insular sclerosis, 227
 Intestinal paresis, 212
 Intrahepatic gall-stones, 279

J

- Jaws, surgery of, 265

K

- Kidney diseases, 222, 247
 Kimura, J. K., Investigation of the portio vaginalis of the uterus in relation to conception, 171
 King, J. M., Treatment of pellagra, 58

L

- Large intestine, surgery of, 270
 Lavage, 207
 Leprosy, 238
 Leukæmia, 217
 Leukoplakia, 16
 Lumbar puncture, 35
 Lung complications after operation, 255

M

- Measles, 238
 Medicine, progress of, 228
 Meningitis, 199, 236
 Menstruation, hygiene of, 145
 Metabolic diseases, 202, 240
 Miscellaneous topics, 188
 Much's reaction, 250
 Mucous colitis, 95
 Mumps, 239
 Musser, John H., Progress of medicine during 1909—medicine, 228
 Myocarditis, 221
 Myxœdema, 205

N

- Nervous diseases, 224, 250
 system, 32
 syphilis of, 32
 Neuralgia, trifacial, 225
 Neurasthenia, 225
 Neurology, 157
 Nichols, J. B., The tuberculins and their diagnostic and therapeutic use, 62
 Noguchi, Hideyo, Further studies on the serum diagnosis of syphilis with especial reference to the antihuman hæmolytic system, 22
 reaction, 11, 22

O

- Obesity, 206, 242
 Oedema of the lungs, 215
 Oesophagus, surgery of, 292
 Operation for gall-stones, 278, 282
 mortality, 278
 Operations on the hepatic duct, 280

P

- Pædiatrics, 149
 Pancreas, surgery of, 282
 Parotitis, 239, 256
 Pellagra, 27, 240
 symptomatology, 42
 treatment, 58
 Pernicious anæmia, 216
 Physiology of the bile, 275
 Plague, 202
 Pleurisy, 215, 247
 Pneumonia, 194
 Poliomyelitis, 237
 Portio vaginalis uteri, 171
 Posterior cholecystenterostomy, 282
 Postgraduate course of study, 188
 Postoperative complications, 252
 Proctolysis, 254
 Progress in gynecology, 126
 of medicine during 1909—medicine, 228
 surgery, 252
 treatment, 198
 Psycho-reaction of Much, 250
 Pulmonary embolism, 256
 oedema, 215
 Purlin metabolism, 76

R

- Respiratory diseases, 212, 247
 Rheumatic fever, 198
 Rising, after operation, 254
 Rocky Mountain fever, 239
 Rupture of the gall-bladder, 275
 of the hepatic duct, 280

S

- Sachs, B., The newer diagnostic methods of syphilis of the nervous system, 32
 Sciatica, 227
 Septic endocarditis, 220
 Serum diagnosis of syphilis, 1, 22, 32
 Silver as an antiseptic, 259
 Smith, A. L., Progress of gynecology and abdominal surgery during the last twenty years, 126
 Special articles, 1, 22, 32
 Spleen, surgery of, 289
 Spotted fever, 289
 Stevens, A. A., Progress of medicine during 1909—treatment, 198
 Stomach, surgery of, 267
 Suppuration and bismuth paste, 102
 Surgery, 102, 120
 progress of medicine, 252
 Symptomatology of pellagra, 42
 Syphilis, 283
 of the nervous system, 32
 serum diagnosis of, 1, 22, 32
 Swift, Homer F., The serum diagnosis of syphilis, 1

T

- Tabes dorsalis, 157
 Tendon transplantation, 265
 Tetany, 227
 Thyroid gland, tuberculous, 120
 Transduodenal choledochotomy, 281
 Transfusion, 249
 Treatment of pellagra, 58
 progress of medicine, 193
 with bismuth paste, 102, 107
 with tuberculin, 62, 72
 Trifacial neuralgia, 225
 Trypsin in tuberculosis, 260
 Tuberculin, 62
 Tuberculosis, 200, 228, 247, 270

- Tuberculosis of the thyroid, 120
 Tumors, 261
 Tuttle, Lucius, Progress of medicine during 1909—medicine, 228
 Typhoid cholecystitis, 276
 fever, 193, 234
 pellagra, 48

U

- Ulcer of the stomach, 208
 Uræmia, 222
 Uric acid formation and gout, 76
 Uterus and conception, 171

V

- Vaccines, 260
 Vomiting, 208

W

- Wassermann reaction, 8, 24, 28, 32, 37
 Watson, J. J., Symptomatology of pellagra, 42
 Wells, H. G., Some recent additions to our knowledge of purin metabolism and their bearing on the problems of gout, 76
 Whooping cough, 197
 Williams, T. A., Tabes dorsalis—its rational treatment in the light of its real pathogenesis, 157

X

- X-rays and bismuth in suppuration, 102

Y

- Young, E. B., The hygiene of menstruation, 145

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